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RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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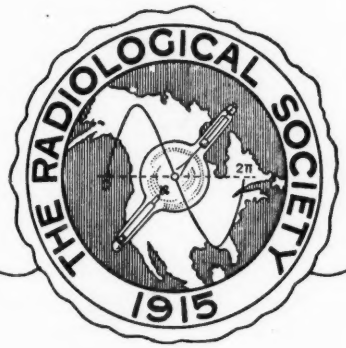

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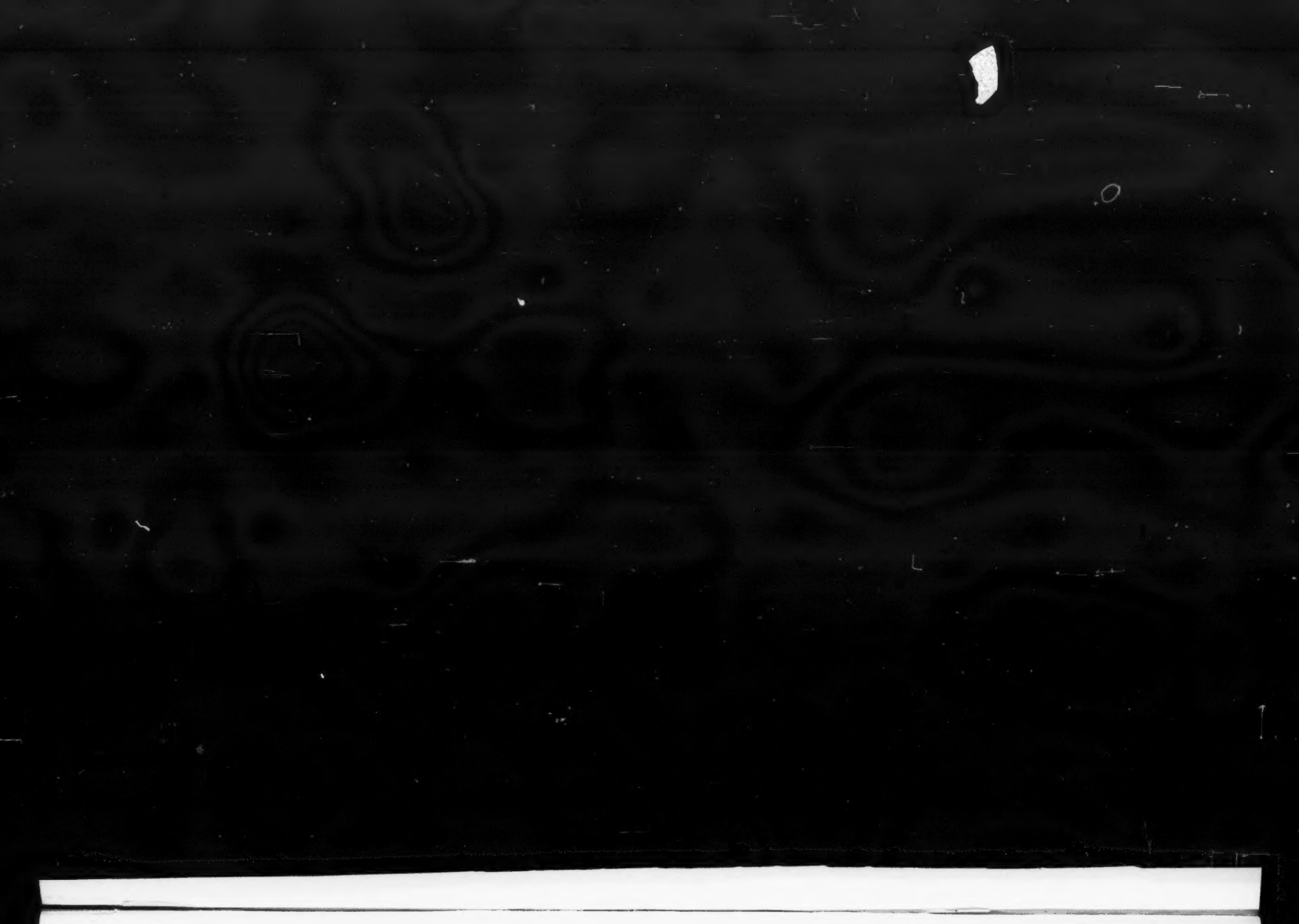

RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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VOL I. SEPTEMBER, 1923 No. 1.

CANCER FROM THE SURGICAL STANDPOINT[1]

By A. J. OCHSNER, M.D., LL.D., F.A.C.S.

Surgeon-in-Chief of Augustana and St. Mary's Hospitals; Professor of Clinical Surgery, Medical Department, State University of Illinois, Chicago, Illinois

AS far back as the history of surgery reaches, surgeons have considered cancer curable in the early stages of the disease, and entirely hopeless after metastases have formed.

The statement concerning cancer which is attributed to Celsus, who lived before and during the beginning of the Christian era, has remained a surgical truth during all of the past centuries.

He is quoted as saying, "Only the beginning of a cancer admits of a cure; but when it is once settled or confirmed, it is incurable and the patient must die under a cold sweat."

It is a fact that when we recall the cases in our personal experience we must agree with Celsus, because it is only in those cases in which we can remove the entire growth that we can hope for a permanent cure.

There are certain regions of the body in which this is less difficult than in others, and it is in these regions (lip, breast, uterus, pylorus, colon) in which the surgeon has recorded most of his successful cases.

Again, there have been certain forms of surgical treatment which have been more certain to remove all of the cancerous tissues in these early cases.

The proportion of permanent cures in cases in which I have removed the tumor by means of the actual cautery has been much greater than those in which I have used the knife, and the only apparently hopeless cases in which I have observed a permanent cure are those in which I destroyed the tumor and the surrounding tissues with the cautery, with the exception, that since we have employed X-ray and radium, we have had quite a series of apparently hopeless cases in which, up to the present time, there has been no recurrence, and a number of these cases seem to have resulted in a permanent cure.

There are four very distinct reasons why the removal of an early cancer by means of the actual cautery, preferably a red-hot soldering iron, should result in a higher percentage of permanent cures than the removal with the knife:

1. The heat is carried far beyond the point at which the tissues are severed and consequently the cancer infection which may exist beyond the line of incision is likely to be destroyed by this heat.

2. We know that if one takes a piece of cancer tissue from the breast of a mouse, cuts this in half, transplants one piece fresh and heats the other to 160 degrees Fahrenheit before transplant-

[1]Read before the Radiological Society of North America at the Annual Meeting, Detroit, December, 1922.

ing, that the former will grow while the latter will not. It is plain consequently that the tissue outside of the cut surface, which has been exposed to the red-hot soldering iron, is not in a condition to act as a cancer graft, while if the tumor is excised with the knife, any portion of the infected tissue beyond will be sure to grow.

3. A knife passing through tissue infected with cancer may act as a means of carrying cancer infection into portions of the non-infected wound. Undoubtedly, the recurrence of cancer in the form of nodules in the scar, following excision of the breast for cancer, is due to implantation of cancer particles with the knife during the operation.

4. In operating with the knife, one is constantly tempted to take away as little tissue as possible, in order to secure a cosmetically perfect result.

One can readily see to what extent these conditions will reduce the chances of thoroughly eradicating a circumscribed cancer infection in case the knife is used in place of the cautery.

Personally I have been convinced for many years as a result of my clinical observations that cancer is due to a specific infection.

The experiments of John Nuzun which have resulted in the isolation of a micrococcus from human cancer which could be cultured and injected in the form of pure cultures into the breasts of mice and dogs, that later on died from metastatic cancer from which the same micro-organisms could be isolated, have still further confirmed me in this belief and have convinced me that the cautery is far superior to the knife for the removal of malignant growths.

It is possible that still better results may be obtained by the use of diathermy, but my experience with this form of treatment is not sufficient to entitle me to an opinion.

We have repeatedly removed carcinomatous breasts or tumors of the neck with the red-hot soldering iron, and have dissected the axillary or cervical lymph glands with the electric cautery in cases which seemed hopeless in which there has been no recurrence for many years. In all of these cases, however, the patients have had after-treatment with X-ray so that we cannot be certain about the part each one of the two methods had in preventing recurrence.

Much progress has been made during the past few years in determining the proper dosage of X-ray and radium by those who have studied the subject both from a scientific and an experimental side and from extensive clinical observation. For this reason I have considered it best for the patient to place the radiologic treatment of my cancer cases entirely in the hands of Dr. Henry Schmitz, an expert radiologist. At the same time, I have never ceased giving these cases my continued interest because it seemed important to give them the benefit of experience obtained through years of observation covering hundreds of cases. I have found that our combined judgment has been valuable to both of us, and to our patients. It seems that in time such teamwork must bring results.

So far, then, we feel certain that quite a number of lives have been actually saved by wide excision, preferably by means of the actual cautery, and that many of our patients are alive to-day who would have died years ago had they not been treated with radium and X-ray, either combined or single.

At the present time, we feel that we should treat all cases of malignant growths with X-ray before operating. We believe that this kills that which has progressed beyond the field of operation, produces immunizing substances and prevents grafting of can-

cer cells with the knife as it may pass through some lymph gland or space beyond the tumor proper.

We are not certain whether it is best to operate immediately after the patient has recovered from the depressing effect of deep X-ray therapy or to wait several days or weeks following this time. At present, we operate within a week after the patient has recovered from the depressing effect of the X-ray or radium treatment in all cases in which it seems as though the patient has a chance for a permanent recovery after the removal of the cancer.

In many cases we have given several courses of X-ray treatment at intervals of from six to sixteen weeks following the operation. A number of these cases are alive after from five to sixteen years.

Since using a more powerful machine we have usually given only one prolonged treatment following the operation. We are not certain as yet whether this plan excels the other. Of late we have regularly given this treatment before instead of after the operation.

In some cases it has seemed as though patients who received one prolonged intensive treatment before the operation and none after the operation were more likely to remain free from recurrence than those who were treated before and after.

It seems wise not to be too positive as yet regarding the adoption of any definite method until all methods have been thoroughly tried in a very large series of cases.

Following the very extensive excision that we make, we observe the case for years in order to discover local recurrence very early because we have learned that by destroying these immediately with the actual cautery, it is sometimes possible to eradicate the cancer infection, while if the recurrent nodule attains any considerable size before it is destroyed with the cautery, the patient is almost certain to die of metastases.

EARLY OPERATION

Many years ago I had a number of experiences which impressed themselves forcibly upon my memory.

I recall a number of cases which came to me so early that with my present experience I am morally certain that they could have been permanently cured if the growth had been promptly removed with the cautery, or in early cancer of the uterus, if the organ had at once been freely removed preferably by severing the vaginal attachment with the cautery.

In these cases three blunders resulted in the death of the patient:

1. Waiting to make certain that the diagnosis of cancer was correct. By the time this was accomplished, metastatic infection had occurred and the case was hopeless.

2. Scrapings or sections of the suspicious tissue were examined microscopically. At that time, these specimens were removed with the knife or the curette. These patients died regularly from metastases. Not a single case in which the scrapings or the piece excised with the knife showed the presence of cancer has escaped death as a result of metastatic infection.

3. The tumor was removed with the knife, care being taken to obtain a good cosmetic result. These patients had local recurrence and later metastases, but they all died.

The unfortunate circumstance lies in the fact that these blunders were made in just those cases that had almost a perfect chance for permanent recovery had they been treated decently.

Excision of portions of suspicious growth to confirm a diagnosis of malignancy has been insisted upon by some and condemned by others and the

arguments on both sides are so well known that they need not be repeated here. The only case in which I am willing to expose the patient to the danger of dying, as a result of metastases caused by excision of a portion of a growth suspected of malignancy, is one in which the removal of a growth, possibly but not probably malignant, would result in the unnecessary sacrifice of a limb or an important organ or would produce an extensive deformity. In these cases the piece removed should be sufficiently large so that a positive diagnosis can be made, and the removal should be accomplished by the use of the electric or the Paquelin cautery so that the lymph channels and blood vessels will be sealed, and will not carry cancer fragments to distant parts. Moreover in these cases, the entire tumor should be removed so that portions from different parts can be taken for examination because frequently microscopic sections from one part may fail to show malignancy in growths in which other portions are plainly malignant.

Moreover, the examination should be made at once, and if the result does not absolutely establish the fact that the growth is benign, the operation should be carried out at once. In my experience, many cases in which the benignity of a growth could not be established positively by the preliminary microscopic examination, have proved to be malignant on thorough examination. In many excisions of early cases of cancer, I have for many years followed the rule to remove at the first operation as much tissue as one usually expects to remove after the first recurrence following the primary operation without regard to the cosmetic result. As a matter of fact, it does not matter much how badly the wound looks after a really extensive removal. One can always get a better cosmetic result later on than one can following an operation for recurrence.

If one recalls the sayings of the ancients regarding epithelioma, "Be unwilling to touch me" (*nolle me tangere*), it is easy to understand why one should make an extremely wide excision, and also why this excision should be made with the cautery.

The ancients had observed that these skin cancers were fairly certain to remain stationary for a long time if not touched, and that when once started in their growth that the case became hopeless.

How often have we not seen a pigmented nævus remain apparently perfectly harmless until it was accidentally crushed or incompletely removed when it would spread violently, producing great numbers of metastatic tumors which would in a relatively short time destroy the life of the patient.

All tumors in their incipiency seem to have a surrounding area which prevents their invasion of adjacent tissues except by very slow infringement. Let this immunizing area be disturbed by a trauma or by the surgeon's knife, and there is at once rapid progress with the formation of metastases.

We saw this early in our experience. Some thirty years ago when osteopathy first appeared many cases of cancer of the breast that came to the hospital had their tumors manipulated vigorously by the osteopathic practitioners, and most of them had metastatic tumors when they came to our clinic. Later these practitioners learned not to manipulate apparently malignant growths, and as a result this complication became less common.

In our enthusiasm over results of treatment of early cases of cancer, we must not forget the far greater importance of seeking for means of prevention.

In order to appreciate the importance of this, we must try to visualize the ravages of cancer in this country.

We are paying billions of dollars for our portion of the expenses of the late war and other billions to prevent future wars. The number of deaths from wounds inflicted upon American citizens in the late war was somewhat less than 50,000. The number of deaths from cancer since the close of the war has been more than 300,000 in the United States, according to reliable statistics.

Unless we find some means of preventing cancer, we must expect to lose a number of citizens of the United States every single year, greater than the total number of lives lost in our army during the late war.

A portion of this loss can be eliminated if we continue our propaganda, so that a constantly increasing proportion of cases come under our care before metastases have formed, and the family physician and surgeon appreciate more and more the harmful effect of temporizing, and the great importance of making an absolutely radical removal the moment the patient comes for examination. The appreciation of the whole profession of the value of X-ray and radium applied according to the directions of a competent, thoroughly scientific, experienced radiologist will help greatly in saving many cases that are now hopelessly lost.

Speaking of cancer from the surgeon's standpoint, I would suggest the following conclusions:

1. The most important work the surgeons and the whole medical profession can do is to develop methods for the prevention of cancer.
2. Eliminate all sources of irritation.
3. Eliminate all sources of filth.
4. Eat only clean food or cooked food.
5. Encourage patients to come early for examination.
6. Make a careful, thorough examination in every case.
7. When in doubt, remove the growth as thoroughly as though you were not in doubt.
8. Remove a malignant growth at the primary operation as widely as you would expect to remove it after the first recurrence.
9. Use the actual cautery whenever it can be used.
10. Always work in conjunction with a competent radiologist.
11. Observe every patient at stated intervals after the operation, and destroy any recurrent nodule at once with the cautery or with radium.

FURTHER OBSERVATIONS WITH THE AUTHOR'S SPHENOID LINE AND HIS POSITION FOR MAKING RADIOGRAPHS OF THE PARA-NASAL SINUSES[1]

By AMEDEE GRANGER, M.D.

"Officier d'Academie;" Director of the X-Ray Department of the Charity Hospital, New Orleans; Professor of Radiology, Tulane University, Post-Graduate Medical School

THE author has made a very careful study of the radiographs of all the cases examined for evidence of disease of the para-nasal sinuses in his office and in his Department at the Charity Hospital, and it is most gratifying to him to be able to report that the work shown to this Society last December in Detroit, has been fully confirmed and that after six months' further trial of the position and angles advocated at that time his conclusions remain the same.

The work done at the Charity Hospital is especially conclusive because in that 1,200-bed State institution, located in the City of New Orleans, with its large cosmopolitan population including some 150,000 negroes and foreigners, we have to deal with a very ignorant class of patients, some of whom hardly understand English, and the great variety of types and shapes of heads which we have to ray, would delight any anthropologist.

In spite of all these difficulties, it has been possible by making use of the author's head rest and of his alveola-glabella position of the head to obtain postero-anterior views of 107° and 23° angles that are strikingly similar in appearance and which show plainly in every case the important sphenoid and ethmoid landmarks described at the Detroit meeting.

We have learned to lay more stress than ever on the 107° angle view, making use of the 23° angle view to confirm the findings obtained from the former and to show the frontal sinuses.

The importance of the G line which forms the upper boundary of the sphenoid sinus in the postero-anterior 107° angle view has been fully and conclusively demonstrated. We were able repeatedly by a careful study of that line and of the density of the shadow of the sphenoid region which lies immediately below it, to make diagnosis, confirmed at operation, of acute sphenoiditis (when there was pus in the sinus); polypoid sphenoiditis; and chronic suppurative sphenoiditis with osteo-plastic changes.

In several cases of unilateral optic neuritis when the teeth, the tonsils, the sinuses (maxillary, frontal ethmoids), and other usual sources of infection had been excluded, and the cause was still undiscovered, and in one case of attacks of severe hemicrania recurring at irregular intervals during a period of several years, we made a diagnosis of hyperplastic sphenoiditis on the affected side based on alterations of the G line to be described in detail later.

Unfortunately not one of these patients would submit to operation and although it can hardly be a coincidence that in these 12 or more cases definite evidence of disease was found only in the sphenoid sinus on the same side as the optic neuritis and the hemicrania, these diagnoses still remain to be corroborated by the opening of the sphenoid sinus.

ACUTE SPHENOIDITIS (left side). The G line is absent on the left side (Plate I, Fig. 1) and the shadow of the region (sphenoid sinus) below the G line and above the C line is slightly increased in density. If both sphenoid sinuses contained pus the G line would be absent or very indistinct on both sides and the shadows of both sphenoid

[1]Read before the Radiological Society of North America at the Mid-annual Meeting, San Francisco, June, 1923.

Acute Sphenoid | Polypoid Sphenoid | Hyperplastic Sphenoid | Chronic Suppurative Sphenoid

PLATE I. Typical posterior-anterior views, 107° angle of heads showing the alteration of or the absence of the G line, and the density of the sphenoid region. (See Key on this page.)

regions (space directly below the normal site of the G line) would be slightly increased in density. If both sphenoid sinuses were filled with thick pus the G line would be absent and the sphenoid regions would be seen as a dense shadow with a distinct upper convex outline corresponding to the course of the G line in normal sphenoids.

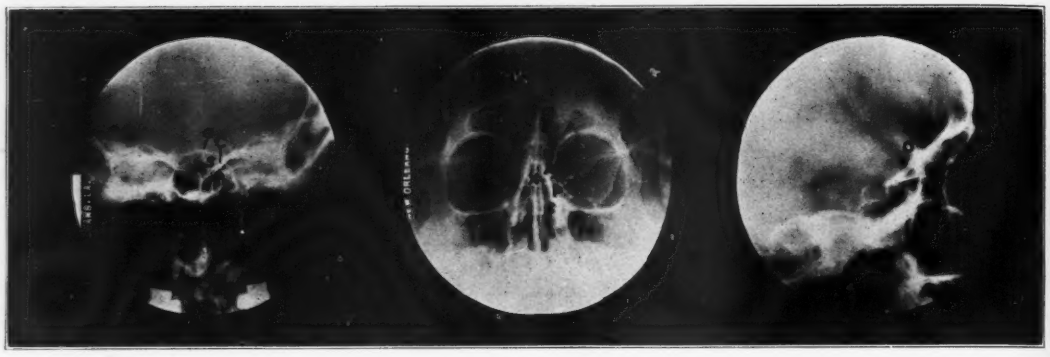
POLYPOID SPHENOIDITIS (right side). The G line is absent on the right side (Plate I, Fig. 2) and the shadow of the sphenoid region shows a marked increase in density with convex upper border corresponding to the course of the G line in normal sphenoids. The shadow of the right ethmoid region also shows a marked increase in density. If both sphenoids are involved these changes are seen on both sides.

The history of the patient and a careful rhinological examination will readily differentiate the radiological picture of this condition from that of an acute empyema of the sphenoid sinus complicating acute or chronic ethmoiditis which it may resemble.

HYPERPLASTIC SPHENOIDITIS (right side). The G line is thicker on the right side (Plate I, Fig. 3) but it is less sharply defined than in normal sphenoids or in chronic sphenoiditis with osteo-plastic changes. In some cases, the G line besides being less sharply defined is both thicker and denser on the diseased side. In still other cases the G line is broken, less sharply defined, and shows here and there areas of increased density and thickness on the diseased side. In all the cases of this type which came under his observation, the G line showed alterations on one side only, and little or no changes in density were seen in the subjacent region (sphenoid sinus) and in the ethmoid regions.

CHRONIC SPHENOIDITIS WITH OSTEO-PLASTIC CHANGES (right side). The G line is more distinct and thicker on the right side (Plate I, Fig. 4) and the subjacent region (sphenoid sinus) is denser than normal. In the cases of

KEY TO ILLUSTRATIONS:—*A*, anterior ethmoid cells; *F*, frontal sinus; *G*, G line, upper boundary of the sphenoid sinus in the 107° angle view; *M*, maxillary sinus; *O*, anterior boundary of the sphenoid sinus in the lateral view; *P*, posterior ethmoid cells; *S*, sphenoid sinus; *X*, upper boundary of the sphenoid sinus in the 23° angle view.



Posterior-anterior view, 107° angle | Posterior-anterior view, 23° angle | Lateral view

PLATE II. Normal sphenoid and ethmoids in a living subject. (See Key on page 7.)

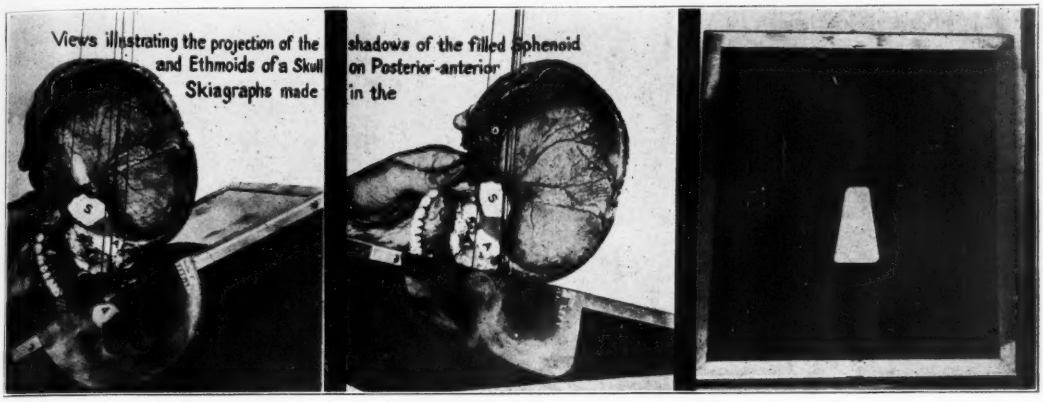
this type which he saw, the ethmoid regions were denser than normal and their trabeculæ and walls were thicker.

When the G line showed none of the alterations described above and was clearly outlined (Plate II, Fig. 1) we gave it as our opinion that there was no disease of the sphenoid sinus. These negative sphenoid findings were confirmed in all the patients suffering from diseased ethmoids who were operated upon, and in all the patients with or without diseased ethmoids who were kept under observation and treatment.

We have discontinued the use of the lateral view for the diagnosis of disease of the sphenoids and ethmoids because we have become convinced that it helped little, if at all, in determining the presence of increased density of those regions. But we are certain that it is useful to determine the size of the sphenoid sinus, its depth and length, and the presence of adventitious septa, and the distance from the sub-nasal point (base of the nasal spine) to the anterior sphenoid wall.

The sphenoid sinus in Skull E (Plate III, Fig. 1) is of unusual length, extending beneath and beyond the floor of the sella turcica. In a patient with such a sphenoid sinus, if the operator was not aware of the true condition he

PLATE III.



23° angle position 107° angle position The author's head rest.

PLATE IV.

would have cause for worry because of the great depth to which his instrument would penetrate.

Skull F was unusual because the sphenoid is subdivided by several septa. Plate III, Fig. 2, shows clearly one of these septa as thick as the normal perpendicular septum which separates the right from the left sphenoid sinus, lying horizontally and dividing both these sinuses into two large cells, an upper and a lower. These adventitious septa would in all likelihood be detected by the careful study of a good lateral view and although this information might be of little value in so far as the operation itself is concerned, it would be of unquestionable assistance in making a prognosis as the chances of a successful operation on such a sphenoid, if diseased, would be doubtful indeed.

For these reasons we believe that a lateral view of every case of diseased sphenoid going to operation should be made, and after careful study of the negative, a detailed report of the findings should be sent to the oto-laryngologist.

A FURTHER STUDY OF THE DESSAUER CHARTS[1]

By ARTHUR W. ERSKINE, M.D., CEDAR RAPIDS, IOWA

THE investigation by Dr. Dessauer of the distribution in water of X-rays produced under varying conditions, and the presentation of his results in the form of the graphic charts bearing his name, have been of inestimable value to all roentgenologists. From the charts it is possible to determine, roughly, at least, the

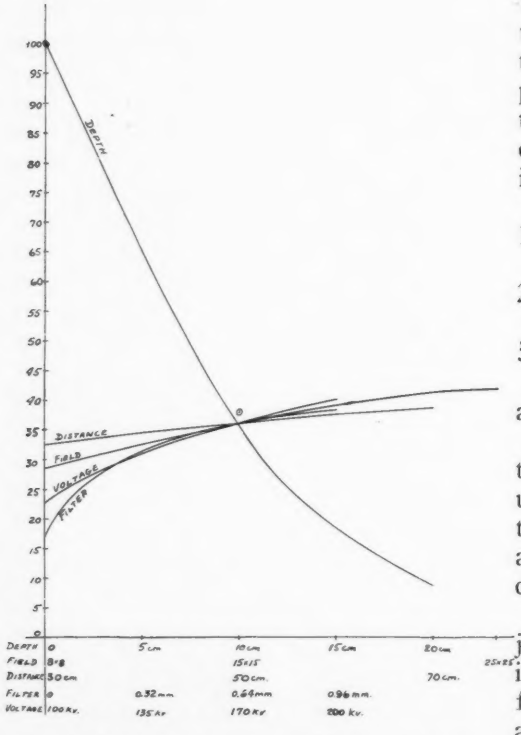


Fig. 1. Specimen graph showing method

percentage of the original beam of X-rays which reaches any given depth. In constructing the charts Dr. Dessauer used with each voltage the thickness of filter which he believed to be most efficient and economical. We believe that the proper thickness of filter is that which absorbs about 80 per cent of the original beam. Because much of Dr. Dessauer's data was obtained by the use of what we believe to be excessively thick filters, we undertook to repeat his work, using a large number of thicknesses of filter. We also made a study of enough variations in the other factors, size of fields, anode surface distance, and voltage, to enable us to determine, by interpolation, the distribution of X-rays produced with any possible combination of factors of technique. We found it necessary to construct 144 charts using the following variations in factors:

1. Four filters, varying from none to 1.28 mm. of copper.
2. Four voltages, 100, 135, 170, and 200 kilovolts.
3. Three anode surface distances, 30, 50, and 70 centimeters.
4. Three sizes of field, 8x8, 15x15, and 25x25 centimeters.

Great pains were taken to measure the voltage and to keep it constant. We used a sphere gap, corrected for altitude, before and after each experiment, and as a further check, an especially calibrated kilovolt meter.

The copper used for filters was subjected to chemical analysis to determine its purity, and its thickness was carefully measured by a micrometer, and also determined by the relation between its area and weight.

To measure the relative ionizing effects of the rays at the different depths and parts of the field we used a gold leaf electroscope, connected by an enameled wire to a small aluminum ionization chamber. The wire was supported by solid sulphur in a lead-lined brass tube. In order to eliminate personal error in measuring the depth of

of reducing error in data by plotting all variations in technique.

[1]Read before the Radiological Society of North America at the Mid-annual Meeting, San Francisco, June, 1923.

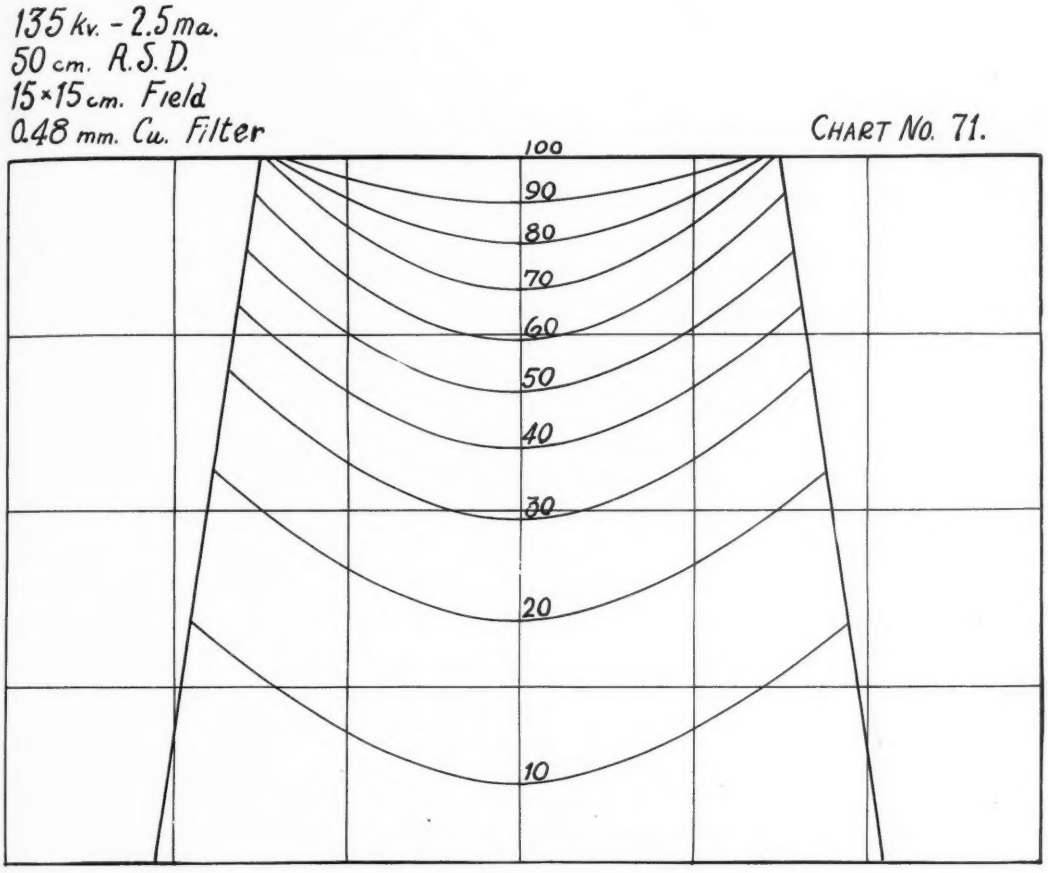


Fig. 2. Chart constructed from measurements when the following factors were used: Kv. 135., ma. 2.5, A.S.D. 50 cm., Field 15x15, Filter 0.48 mm. Cu.

the ionization chamber in the water, we used a simple mechanical device to fix the chamber in the same positions in the phantom for each series of readings.

The center measurements were made with the ionization chamber at the surface of the water and at depths of 5, 10, 15, and 20 centimeters, and the side measurements at the surface and at depths of 10 and 20 centimeters. By dividing the number of seconds required to discharge the electroscope with the ionization chamber at the surface by the number of seconds required for discharge with the chamber at the various depths, we determined the depth dose percentage at several points, from which we plotted a curve. Because of the large number of measurements made, it was also possible to plot percentage curves according to variations in voltage, filter thickness, anode surface distance, and size of field, and to use them to discover inaccuracies and reduce errors. We believe that the error in the charts is less than 2 per cent. The accompanying tables from which the charts were constructed show the adjusted depth percentage corresponding to all the variations in technique.

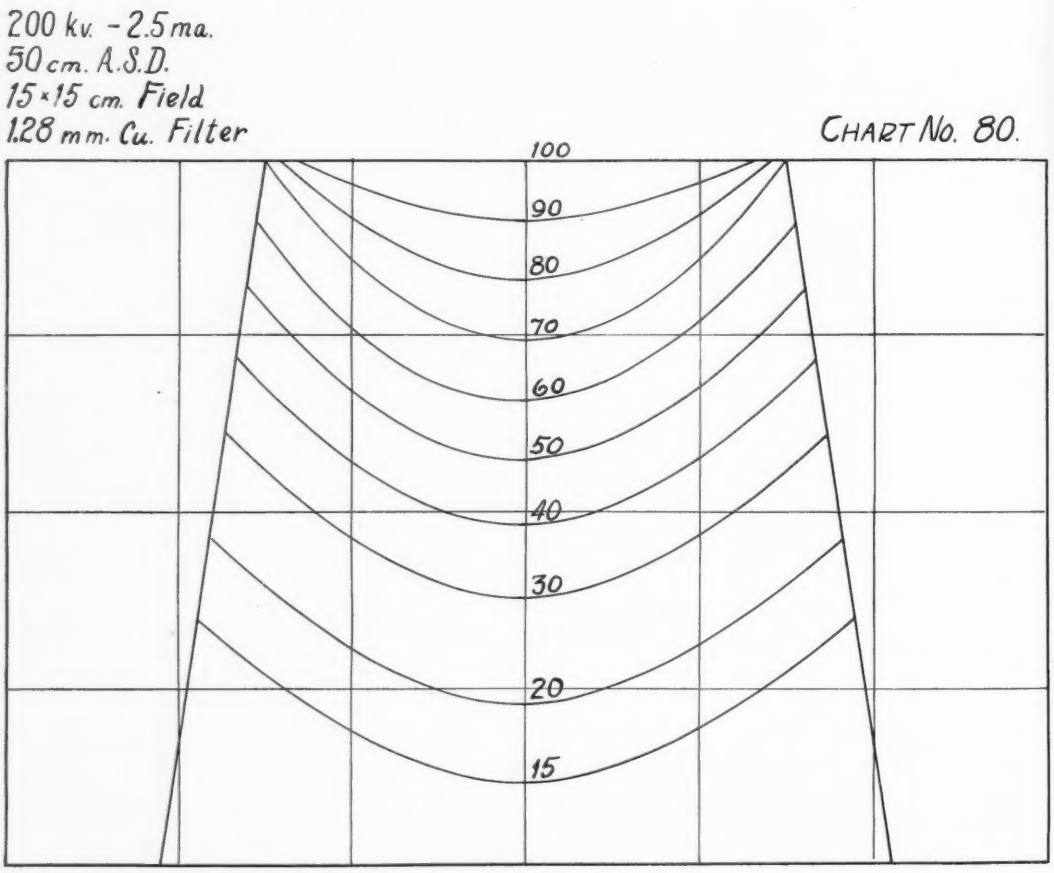


Fig. 3. Chart constructed from measurements when the following factors were used: Kv. 200., ma. 2.5., A.S.D. 50 cm., Field 15x15, Filter 1.28 mm. Cu.

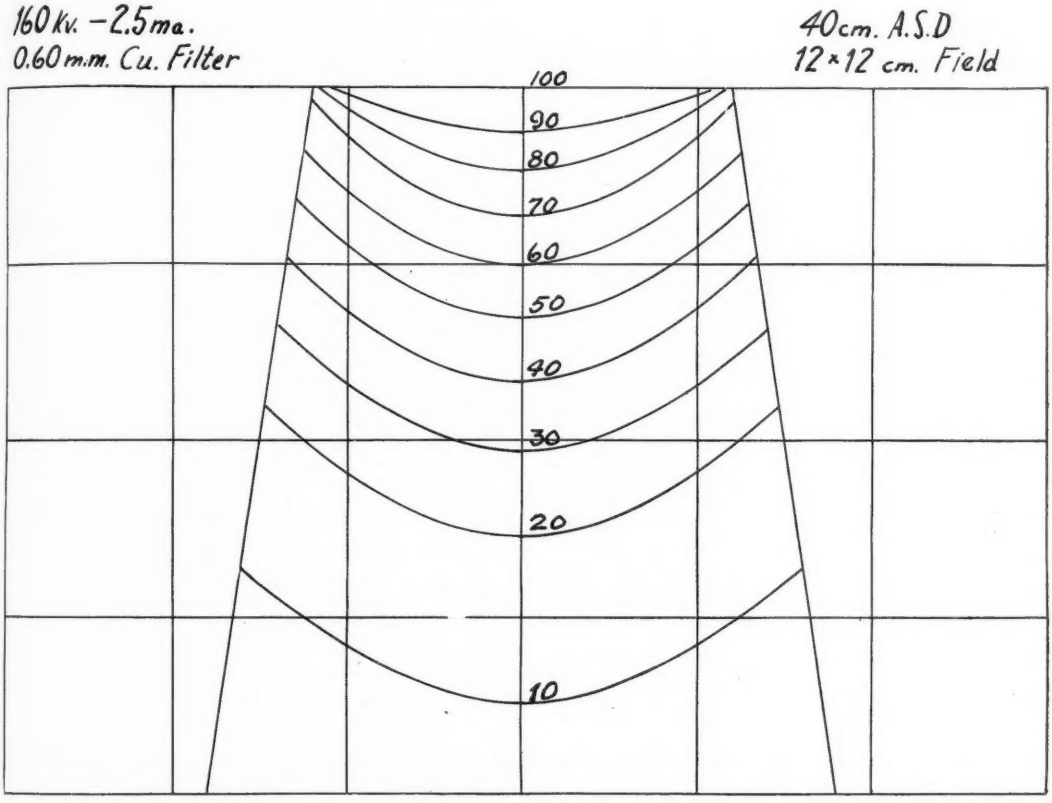


Fig. 4. Chart constructed by interpolation according to the following factors: Kv. 160., ma. 2.5, A.S.D. 40 cm., Field 12x12, Filter 0.6 mm. Cu.

(See Tables I, II, III, and IV on pages 14 and 15.)

TABLE I

100 kv.—2.5 ma.

Filter	Position Ion. Ch.	30 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field	50 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field	70 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	22.0	26.6	28.7	24.0	27.5	31.0	25.0	30.1	32.5
None	10 cm.	6.4	9.0	10.0	7.5	9.5	11.0	8.0	10.5	11.6
	15 cm.	1.8	3.0	3.5	2.0	3.3	3.7	2.5	3.6	3.8
	20 cm.	0.5	1.0	1.3	0.6	1.1	1.7	0.7	1.5	1.8
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	37.0	43.0	45.2	39.5	44.3	49.5	40.5	47.3	51.5
0.16 mm.	10 cm.	12.0	16.0	18.0	14.0	17.0	20.5	14.5	19.3	22.0
copper	15 cm.	4.3	6.6	7.5	5.3	7.0	8.8	5.8	8.0	9.5
	20 cm.	1.3	2.5	3.1	1.8	2.8	3.7	2.0	3.7	3.9
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	42.5	49.0	52.0	45.0	50.5	56.0	46.0	54.0	58.0
0.32 mm.	10 cm.	15.5	21.0	24.0	17.9	22.6	25.8	19.0	24.5	27.1
copper	15 cm.	5.7	8.5	10.2	6.8	9.5	11.8	7.5	10.8	12.5
	20 cm.	2.2	3.8	4.5	2.6	4.0	5.0	3.2	4.8	5.4
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	49.0	56.0	60.0	52.0	58.5	64.3	53.0	61.6	66.0
0.64 mm.	10 cm.	19.5	25.0	27.2	21.5	26.8	32.0	22.0	29.5	33.2
copper	15 cm.	7.0	11.0	13.5	8.8	12.6	15.7	9.3	14.2	16.7
	20 cm.	2.6	4.5	5.2	3.3	4.8	6.3	3.8	5.7	6.7

TABLE II

135 kv.—2.5 ma.

Filter	Position Ion. Ch.	30 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field	50 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field	70 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	29.8	35.5	38.3	31.5	36.8	40.8	33.5	39.5	42.5
None	10 cm.	9.5	13.0	15.4	10.0	14.4	16.9	10.5	16.3	17.9
	15 cm.	3.7	4.9	6.0	4.1	5.5	7.2	4.3	6.5	8.0
	20 cm.	1.0	2.0	2.6	1.3	2.4	2.8	1.7	2.7	3.0
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	42.0	47.3	53.0	44.6	51.4	58.2	46.0	55.6	60.0
0.16 mm.	10 cm.	16.2	21.5	25.4	18.3	24.0	28.0	19.5	26.6	29.5
copper	15 cm.	6.1	8.9	11.0	7.3	9.9	12.0	8.0	11.6	12.7
	20 cm.	2.6	4.2	4.8	3.5	4.6	5.6	3.8	5.2	6.2
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	51.5	58.0	61.2	54.4	60.5	66.7	56.0	64.5	69.5
0.48 mm.	10 cm.	21.5	28.2	32.0	24.4	31.0	36.5	25.5	33.5	38.5
copper	15 cm.	10.0	14.0	16.2	10.9	15.3	18.0	12.0	17.0	19.0
	20 cm.	4.0	5.5	6.8	4.7	6.3	8.3	5.0	7.3	9.0
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	55.5	62.5	67.0	58.4	65.2	71.5	59.1	60.0	74.5
0.80 mm.	10 cm.	24.5	31.0	35.7	27.3	34.0	41.0	28.0	37.0	42.0
copper	15 cm.	9.0	13.6	17.8	11.5	16.0	21.0	12.3	19.0	21.6
	20 cm..	4.3	7.0	8.5	5.5	8.0	10.0	5.9	9.0	10.5

TABLE III

170 kv.—2.5 ma.

Filter	Position Ion. Ch.	30 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field	50 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field	70 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	33.3	39.7	43.0	35.2	41.5	45.5	37.5	44.5	47.5
None	10 cm.	11.6	15.5	18.3	13.2	17.1	20.0	14.2	19.2	21.0
	15 cm.	4.5	6.8	8.5	5.6	7.7	9.5	6.2	9.0	10.0
	20 cm.	1.8	3.1	3.8	2.2	3.7	4.5	2.8	4.0	4.7
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	51.5	58.5	62.7	54.0	61.5	66.3	55.5	64.2	69.0
0.32 mm.	10 cm.	22.0	28.5	32.5	24.6	31.5	36.5	25.6	34.5	38.0
copper	15 cm.	9.0	13.4	17.0	10.6	15.5	19.0	11.5	18.0	20.7
	20 cm.	4.0	6.5	8.0	5.0	7.5	9.3	5.7	8.8	9.7
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	55.0	62.1	67.0	58.2	65.7	71.8	60.0	69.5	74.0
0.64 mm.	10 cm.	25.5	32.5	37.9	28.5	36.0	42.0	29.6	38.9	44.2
copper	15 cm.	10.5	15.8	19.7	12.8	18.5	22.3	13.5	20.8	24.2
	10 cm.	5.0	7.6	9.5	6.0	9.0	10.8	6.7	10.0	11.5
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	56.7	64.0	69.8	60.0	67.8	74.5	61.2	72.0	77.0
0.96 mm.	10 cm.	27.0	34.3	41.0	31.0	38.7	46.5	32.0	42.8	47.5
copper	15 cm.	11.5	16.7	20.5	13.5	19.0	23.5	15.0	21.9	25.4
	20 cm.	5.5	8.5	10.4	6.8	9.7	11.8	7.5	11.0	12.8

TABLE IV

200 kv.—2.5 ma.

Filter	Position Ion. Ch.	30 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field	50 cm. A.S.D. 8x8 Field	15x15 Field	25x25 Field	70 cm. A.S.D 8x8 Field	15x15 Field	25x25 Field
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	35.0	42.0	45.7	37.5	44.5	49.3	40.0	47.5	51.0
None	10 cm.	13.4	17.0	20.5	15.5	19.4	22.2	16.6	21.5	23.1
	15 cm.	5.0	7.7	9.1	6.0	8.5	10.4	6.6	9.7	11.2
	20 cm.	2.0	3.0	4.0	2.5	3.4	4.7	2.7	4.4	5.0
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	53.0	60.0	65.2	55.5	63.5	69.0	56.8	67.0	71.0
0.32 mm.	10 cm.	24.0	30.4	34.5	26.0	32.3	38.0	27.2	36.0	39.8
copper	15 cm.	10.4	14.9	18.2	12.0	16.8	20.4	13.0	19.0	21.2
	20 cm.	4.5	7.0	8.4	5.6	7.9	9.5	6.3	9.2	10.0
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	56.7	65.2	71.5	60.8	69.3	75.5	62.5	73.2	77.8
0.8 mm.	10 cm.	27.1	35.0	42.0	30.8	40.0	46.5	32.5	43.5	48.0
copper	15 cm.	11.8	16.7	21.5	13.8	19.8	24.0	14.9	22.4	25.0
	20 cm.	5.6	8.5	10.5	7.0	9.5	12.0	7.5	11.0	12.5
	Surface	100	100	100	100	100	100	100	100	100
	5 cm.	59.5	67.7	73.0	64.0	70.7	77.0	65.5	74.5	78.5
1.28 mm.	10 cm.	28.0	37.1	43.0	32.5	41.3	49.0	35.0	45.0	51.0
copper	15 cm.	12.2	18.0	23.0	14.0	21.0	26.0	16.2	24.0	27.0
	20 cm.	6.0	9.5	11.5	7.5	10.8	13.0	8.5	12.0	14.0

TREATMENT OF CANCER OF THE BREAST BY DEEP RADIATION AND SURGERY—A RATIONAL METHOD ACCORDING TO PRESENT-DAY KNOWLEDGE[1]

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IN order to discuss intelligently the question of the relative values of various methods of treatment, let us briefly recall some facts and theories that laboratory experimentation and clinical experience have developed in the centuries of struggle against this decimating disease.

1. *Anatomy.* A very brief reference to the anatomy of the breast, merely mentioning the circulation, will suffice at this time.

The blood supply is very complicated, because of the location of the organ. It is provided for by the innominate and subclavian, the internal mammary, and rami of the intercostal arteries, accompanied by their veins and lymph vessels. The latter drain either into the auxiliary supra- and infra-clavicular lymphatic glands, or, directly into glands which are located close to the mediastinum, and follow the course of the thoracic duct.

This is a most important factor, not only because of the possibility of metastases to the chest wall, but also because of the likelihood of early implantations of foci of carcinoma within the intrathoracic region which cannot be reached by the surgeon's knife.

Various modifications of the lymph drainage of the breast have been demonstrated, and, according to Handley's permeation theory, they account for differences in distribution of metastases. Thus, in the anastomosis with the opposite side, an appreciation of metastases occasionally occurring in the opposite supraclavicular fossa and the opposite breast and axilla is afforded.

Handley stresses the importance of the network of lymph channels which lie above and below the pectoralis fascia, send out branches vertically to the skin and chest wall and connect with the epigastric region, in addition to the other regions mentioned.

The axillary lobe of the mammary gland extends far into the axilla, and in a radical operation necessitates an extensive incision. This region frequently is the primary seat of the tumor. This extension of the gland is generally underestimated, because we are not used to seeing coronal but vertical sections. Only the former, however, distinctly show that parts of the gland extend under the skin in the form of flat discs, and that isolated lobules lie far away from the main gland.

2. *Pathology and Clinical Appearance.* For the sake of completeness we shall touch on the gross pathology of the condition but avoid details.

We all remember the large tumors which cause more or less marked increase in the size of the gland and usually grow rapidly, metastasize early, soon ulcerate, frequently bleed seriously, and rapidly sap the life of the host, the medullary carcinoma. Here there are large aggregations of rapidly multiplying cells and but little fibrous stroma.

Then, by contrast, there is the small hard one, which shrinks the gland, grows slowly, often appears stationary, and metastasizes late. Like scar-tissue it retracts the skin in places, producing an irregular dimpling, or it retracts the nipple, causing the old classical sign of inversion. Mere inspection is often sufficient for diagnosis. In this the cells are replaced by fibrous tissue. Handley says the lymphatic vessel becomes so distended with cells that it bursts, inflammatory action takes place, and after a time the lymphatic vessel becomes a fibrous cord, "perilymphatic

[1]Read at the Mid-annual Meeting of the Radiological Society of North America, San Francisco, June, 22, 23, 1923.

fibrosis." He describes this as a completed cycle of cancer growth, where Nature cures by fibrosis the older part of the growth, while the microscopic "growing edge" progresses unimpeded by the normal tissues, till its progeny become too numerous for the lymph vessel and the above part of the cycle takes place, while the young "growing edge" constantly advances.

Then we have the disagreeable picture of cancer *en cuirasse* with its diffuse skin infiltration, swellings, different shades of redness, with later small superficial nodules and ulcers, causing much pain and discomfort.

In any of these patients we may find by roentgenographic examination, secondary nodules in the mediastinum, lungs, or bones.

Finally there is the unfortunate operated patient with recurrences throughout the whole field of operation and often in the chest and bones. Many times she has an enormously swollen arm from which she suffers tortures, and from which there seems to be no escape. These patients are a source of great worry to the surgeon and attendants and the only escape from that worry on the part of the surgeon seems to have been to recommend the X-ray man. For a score or more of years, the radio-therapeutist has carried the responsibility of these awful by-products of surgery.

The beginning of all these conditions is, as we all know, a small nodule or lump, or scarcely definable infiltration, attached early to the skin, or to the deep fascia, or the chest wall, or, in many cases, apparently not attached to any underlying or overlying structure.

3. *Diagnosis.* The early diagnosis is often attended with great difficulty. Small growths diagnosed as benign, on microscopical examination often prove to be malignant, and *vice versa.* Then too, we have had operated cases with recurrences come to us with a microscopical report of benignancy at the time of operation.

The malignant tumor requires wholly different therapeutic measures from those necessary for a benign fibroma, fibro-adenoma, tuberculosis, lues, cyst or the so-called chronic cystic mastitis. The differential diagnosis of the first two from cancer is comparatively easy, but the latter four in most cases lead to conditions often closely simulating cancer. The malignant pathological changes developing in such conditions are poorly demarcated from surrounding healthy tissue. Tuberculosis, lues, cysts, and chronic cystic mastitis also extend by infiltration, cause enlargement of glands, and in the duration of their growth, absence of pain, as well as by their appearance and form closely simulate cancer.

Dr. Bloodgood, however, at a cancer clinic in Detroit last year, stated that cysts of the breast and chronic cystic mastitis do not become malignant any oftener than any other breast, that they should and can be diagnosed and should not be operated upon. It would seem to be the part of wisdom for the present to treat all these lesions of uncertain diagnosis as guilty of malignancy until they prove themselves otherwise.

Careful histories and physical examinations should always be made. The latter should include, routinely, blood examinations and roentgen examinations of the chest in the beginning and at intervals after treatment. The bones above the knees and elbows should also be examined, especially in advanced cases.

We think in view of Dr. Maud Slye's convincing work, more careful histories concerning heredity should now become of great importance.

4. *Treatment.* Medical history for the past twenty-five hundred years has recorded the attempts to cure cancer of the breast—known in Roman days

as "fungus of the breast"—by means of surgery.

Medical history also records the fact that about twenty-seven years ago, X-ray and, a year later, radium were discovered.

In the last seventy-five years, since the introduction of anæsthesia and of antiseptics, the science and art of surgery have developed almost to perfection. The surgical treatment of cancer of the breast has attained such a high degree of perfection, it is a common saying that no further improvements in the technique of the operation can be made. In spite of this, the very best statistics given for successful surgical treatment of cancer of the breast, taking the cases as they come, is considerably less than 25 per cent. In the case of the average surgeon, the five-year cures probably do not average 10 per cent. The statistics quoted are greatly dependent upon the personal factor.

It is true some of our most noted surgeons in this country and abroad publish statistics for very early cancer of the breast, without microscopical glandular involvement, which give a percentage of five-year cures, ranging from 70 to 80 per cent plus. This wonderful achievement of surgery is an accomplishment of the last quarter of a century, the entire lifetime of radium and X-ray.

It is quite apparent that when the most perfect surgery possible fails in 80 to 90 per cent of the average run of cases and in 20 to 30 per cent of selected early cases, without glandular involvement, that the surgeon is in need of some outside assistance.

The mutilations from modern surgery of cancer of the breast are very extensive. The morbidity statistics are never included in the mortality statistics. Indeed, they are seldom referred to. Increased longevity may not be desirable if there goes with it increased morbidity. The aim and ambition of medicine and surgery is to preserve the health of people, to make sick people well—not to prolong their misery.

Radiation therapy of cancer by means of X-ray and radium is a development of the past twenty-five years. Indeed, these agents themselves, which have revolutionized all the sciences, have been known to us only about a quarter of a century. Think of the precocity and audacity of X-ray and radium specialists, comparing radiation and surgery in the therapy of cancer! The first paper of one of us on experiences with radium therapy was published twenty years ago, six years after the discovery of radium! We blush to confess it.

As our knowledge of these agents increased, our technique of application rapidly changed and our results improved. Because of these rapid changes in technique, reliable radiation statistics are not available. The personal factor enters here just as in surgery—knowledge, skill, ability, and experience, to have suitable X-ray apparatus and quantity of radium determine results. All these factors in radiation therapy are still in their infancy, and each year has noted marked progress, with change in technique, so that statistics for five years that mean anything are unavailable.

Besides this the science of radiology is so very young—but, withal, we must admit, very precocious. The class of cases the surgeon has permitted the radiologist to treat are: (1) inoperable cases when they first apply for treatment; (2) inoperable recurrences; (3) patients who have been operated upon and are referred later for post-operative prophylactic treatment; (4) exceptional cases in a comparatively early or late stage for pre-operative treatment; (5) rare cases who fear the operation and prefer to take chances with any other form of treatment. The surgeons who give X-ray treatment to their cases prior to operation are extremely few. The propaganda of the Society for the

Control of Cancer is justly or unjustly largely responsible for this. In their literature and the literature of many of the surgeons, we see such paradoxical statements as this: "Surgery is the only cure for cancer. Cases which are too far advanced for operation should be treated by X-ray or radium." These are the cases on which the radiologist has had to build a reputation for the method of treatment he has been trying to perfect.

How can a thoughtful physician deem it possible to cure by local treatment, such as X-ray or radium, no matter how perfect the technique, an inoperable carcinoma which is no more a local condition but is comparable to an advanced constitutional disease? That means to wander in fairy-land or to perform miracles. Surely logical thinking as well as the experiences of the radiotherapists who have attempted the impossible prove the utter fallacy of such expectations. We must face the fact, that in advanced carcinoma, just as much as in tuberculosis, infectious diseases, heart, liver, kidney, and other diseases, and old age, a state is reached in which the resistance and the ability of the body to maintain a metabolic balance is exhausted, and we must set our expectations accordingly. So, we must also accept the assertion that the inoperable mammary carcinomata, and the prognostically equally unfavorable recurrences also are beyond the range of X-ray and radium radiation.

It may seem surprising at first thought that we nevertheless treat these patients, although we are firmly convinced that we cannot produce a permanent cure. Our reasons for favoring this procedure are: 1. The physician should not deprive a patient considered incurable, of all hope by refusing all treatment—to do so would be contrary to our moral and social duty to all mankind. 2. It is extremely difficult, or quite impossible in individual cases, even for the most learned and experienced physician to be sure that in spite of the case being considered inoperable, that all bodily resistance is actually exhausted. There are necessarily borderline cases which still retain a certain amount of reserve body forces. It is these exceptional cases which promise success. They have already been "cured" by radiation for several years, and shine in the statistics of the radiologists. 3. The lives of many of these patients can be saved in a fairly tolerable condition, for two, three or more years, when every month of life means so much to their children. 4. By proper raying, the victims are saved the terrible suffering of extensive ulcerations of the external surfaces, and die from the more tolerable internal involvement.

But one fact is to be emphasized: these patients must not be rayed from a purely physical point of view. If we attempt this, we shall help them very little, if at all, or even harm them.

As already stated, the resistance of these people is exhausted. We must therefore spare them an additional X-ray as well as traumatic insult.

The homogeneous raying of one-half the thorax, or of even larger areas such as a lung, together with the entire mediastinum and the corresponding shoulder girdle, would surely mean trauma which would leave irreparable damage. He who attempts this in already weakened patients must not be surprised at complete failure. The real skill and art of the physician and the roentgenologist lies in his ability to judge how much a patient is able to stand under these circumstances. In these cases, the old method of raying the chest in one plane from several points is undoubtedly justified. Frequent sittings with small or moderate doses from a moderate distance (usually a dose of about two-thirds or three-quarters of the skin erythema dose), which will affect the readily accessible part of the growth, as far

as this is biologically possible, tend to spare the resistance of these patients. In carefully selected cases, we may try to homogeneously ray the supra- and infra-clavicular fossæ and axilla, after careful calculation, but this is as far as we should go. This procedure, however, can be applied only to border-line cases described above, and this is an exception to the rule. To do more, would mean to do harm rather than good.

The foregoing is our conception of the merits of X-ray therapy in advanced mammary carcinoma. On the other hand, how about the cases which are considered operable by the surgeon, and which are brought to the roentgenologist instead of to the surgeon? We must admit that we have had very little experience with such patients, because almost all of them, according to the present state of mind of the public as well as of the physicians and surgeons, are operated upon as soon as they seek medical aid, unless they are humored along by the quack with plasters, salves, and possibly ultra-violet light, until the tumor has become inoperable. Only occasionally have we treated an early case, and yet there are some facts deduced from theory and experiment as well as practice, which point toward success in these cases.

First let us touch briefly upon the evidence we have of immunity in cancer. There are many histological, clinical and biological evidences of immunity.

1. The fibrosis normally occurring in cancer is an attempt on the part of Nature to wall off or strangulate the cancer cells. It may be considered as a local immunity. We see the same process after a definite period following X-ray or radium treatment.

2. Ewing reports strong evidences of local immunity being developed from X-ray or radium treatment, these agents apparently not killing the cells directly, but stimulating a local protection by leucocytosis, plasmacybosis and finally fibrosis.

3. Spontaneous cures of cancer in very rare instances have been reported.

4. Biological experiments on mice with propagated tumors show that mice can be made immune against inoculated mouse cancer by means of X-ray or radium in moderate doses, while their protective forces may be absolutely destroyed by heavier doses. These results have followed after radiation of the tumor tissue before inoculation, and after raying the normal body before the transplantation of tumor.

Experiments with spontaneous tumors in mice have not yielded similar results, however, probably because there must be a vast difference between propagated tumors and spontaneous tumors, and there is also a great difference in the behavior of the animal mechanism toward them.

Dr. Maud Slye's work of many years, on heredity, seems to show conclusively that "cancer and non-cancer tendencies segregate out, are transmitted as such, and are therefore unit characters of heredity. That means that by selective breeding these characters may be manipulated and thereby be planted indelibly in any species, or be eliminated permanently and completely from any species. We either have or have not a mechanism fitted to control proliferation and differentiation in regenerative processes. We inherit or do not inherit, a tendency to cancer."

This field of biological investigation of cancer is a large and promising one and we hope Dr. Slye's experience and her mice, whose unit characters are known to her, may be utilized for further study in connection with X-ray therapy to determine whether or not inherited tendencies may be changed by radiation, and, if so, how and to what extent.

While we should be careful in comparing tumors of different tissues, on

the one hand, and human with animal growths on the other, there is no reason why one should not get the same local and general reactions with breast tumors as with those of any other part of the body, namely, more or less necrosis, according to the technique used, followed by the formation of destructive hormones, cessation of nuclear division to a certain extent, proliferation of fibroblasts, lymphocytosis, and increased immunity against implantation of cancer cells.

It is surprising that with the knowledge of all these changes, the surgeons should not make use of these reactions to a much greater extent, prior to operation.

For fifteen years we have advocated pre-operative raying of cancer as probably being of greater service to the patient than post-operative prophylactic raying.

We have had some co-operation from a few surgeons along these lines, and the results have justified the practice. For several years, in a few cases, pre-operative raying was done according to the older method of crossfire raying of the breast and chest through many small ports, using a ray filtered through six millimeters of glass and six or seven millimeters of leather at about eight or nine inches and a spark gap of nine inches or more. In the past eighteen months, we have used homogeneous rays with two hundred thousand volts, and one millimeter of copper filtration at fifty to sixty centimeters distance. There have been very few early cases. Most of these cases had axillary or supraclavicular glands, or both, and were practically inoperable, but non-radical operations were done one day to three months after radiation. Some of the advanced cases, that is, inoperable cases, are living the three-to-five-year period and longer.

One patient, seventy years old, with scirrhus and deep ulceration of the breast, is living, over four years after the operation, which was performed six months after treatment. Another, having the same type of lesion, had X-ray treatment seven years ago and no operation. She returned recently with a recurrence which has since healed. Another, seventy-one years of age, with a similar condition, refused operation, was treated seven years ago and recently reported with recurrence in the breast, at the site of the old ulcer. She also has metastases in the chest. However, she has had seven years of active and very useful life following the treatment. In another, where the tumor was attached to the skin and was cicatrized, in a patient who had just recovered from a severe attack of uræmia and could not be operated upon, one dose of X-ray was given three years ago and the tumor has remained stationary since. There are many such cases reported, and we have others, but it is impossible to give accurate statistics for reasons mentioned. These few cases simply illustrate what is occasionally done with rays inaccurately measured according to our standards of to-day.

The X-ray treatment we now give to such cases is accurately measured, is of high voltage, homogeneous, and is given in full dosage, usually to two large ports with addition of other ports three or four weeks later, if necessary to cover larger territory.

Such treatment is as serious a measure as a corresponding operation, and we think such patients should be treated and nursed exactly like post-operative cases. They should rest a requisite length of time in bed, be given abundance of fluids to aid elimination of toxins due to the treatment, and they should be carefully watched for many months. We are using diathermy a good deal in cancer cases after X-ray treatment, for several weeks, but cannot yet speak of its value. Iron and arsenic are frequently given, if there is any

tendency to anæmia. In the anæmic cases, we sometimes use blood transfusion with great benefit.

The gynecologists may perhaps have come to the conclusion that in carcinoma of the uterus, surgery, X-ray and radium therapy are equally valuable and act accordingly.

But, until we have a much larger experience in the X-ray treatment of early cases of cancer of the mammary gland, we feel that we are speaking in the best interests of the patient when we urge a combination of pre-operative and post-operative X-ray and surgery. Buried radium may be used in refractory nodules, but we rarely use it in carcinoma of the breast. It should not be used until the field of the growing edge has been covered thoroughly by X-ray.

Our practice has been, in the past, to urge two or three series of X-ray treatments by the older method of treatment and the operation two or three weeks after the last series. With the deep therapy, one series, we feel, will suffice, and the operation may be performed two to four weeks later.

It is not wise to operate earlier than two weeks after the X-ray series, because the shock and toxæmia of the X-ray treatment would then be added to that of the operation and that might be disastrous.

One of us has found no difficulty about the wound healing if made a month after the X-ray series. Dr. Hans Jarre, however, says he has noted in his clinic at Magdeburg, Germany, great interference with healing after the fibrosis changes take place, about three or four weeks after deep X-ray therapy, and he therefore urges operation not later than two weeks after treatment.

We think the surgeon, co-operating with the X-ray man thus, should consider less radical operations. We have seen axillary glands disappear a few weeks after X-ray treatment, followed by simple excision of the breast, without opening the axilla. The X-ray field should be large enough to take in the field recommended by Handley in order to reach the most important part of the growth, the microscopical growing edge, namely, a circle twelve to fourteen inches in diameter, with the site of the original growth in the center.

We must avoid raying too large a surface of the body at a series. We must use due care about repetition of the dose. We must remember we are treating the whole patient, not just trying to kill cancer cells directly. We must keep our patients under close observation and carry out any medicinal, electrotherapeutic, fresh air and sunlight, or ultra-violet light treatment which promises upbuilding of general resistance. We must study the diet and prescribe that which appears to be the best indicated. The skin of the treated area should be looked after carefully. Dodd's solution should be prescribed freely, if there is any sign of dermatitis or intense erythema. Fat should be rubbed into the skin later when the skin becomes dry and brown. The patient must be careful not to scratch or wound or compress by bandages, corsets, etc., the affected skin.

SUMMARY

1. Careful studies of each individual case of cancer of the breast should be made before the treatment is begun. This should include roentgenological examinations of the chest and bones. The patient's elimination and powers of resistance should be ascertained as nearly as possible.

2. The treatment of cancer of the breast should include any and all measures calculated to improve the patient's general health of body and resistance against this specific disease. This may include drugs, sunshine and fresh air,

light therapy, diathermy, serum therapy, etc.

3. Surgery must not longer be depended upon as the single agent of cure of cancer. The surgeon, internist, and radiotherapist should be equal consultants and co-operate in the treatment of cancer of the breast. The radiotherapist must be a man of broad experience in diagnosis as well as treatment. He must be especially equipped with the proper radiotherapeutic appliances and well trained in their proper use.

Surgery will become probably less radical in cancer of the breast and should probably follow proper radiotherapy instead of precede it. This will insure a higher percentage of cures, and is the best we have to offer for cancer of the breast at the present time.

SUCCESSFUL IMMUNIZING AGAINST CANCER[1]

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ONE of the greatest advances in the treatment of infectious diseases has been the securing of a means to increase the resistance of a patient to his infection or the procuring an immunity to the invading organisms. In a similar way, if the problem of malignancy could be solved it would be a decided advance, and the object of this paper is to bring to your attention some encouraging results obtained along this line. This is not an account of any original research of my own but rather an account of the work of others which has been confirmed by myself where it has been shown that an increase in the resistance to cancer may be developed by the inoculation of a patient with his own tumor cells after they have been subjected to a heavy dose of X-rays.

At the very outset of this paper let it be distinctly understood that no wild claims are being made, the only excuse offered for bringing this to your attention at this time being that by so doing it is hoped that interest may be aroused and consequently investigation started. If this is accomplished the true merits as well as the limitations of the method will at once be known and so it will be relegated to its proper place among the other methods of treatment. While scientific investigation is desired, it is sincerely hoped that another thing of promise may not be jeopardized by misguided enthusiasts rushing blindly in and bringing about disappointment and false reports which inevitably result in delaying sober and rational development.

Your program states the subject of my paper to be "The Treatment of Carcinoma of the Breast by the Roentgen Ray," and while I have taken the liberty of changing this title, yet most of the work on humans has been done in cases of breast malignancy. However, the principle should and apparently does apply elsewhere.

Before actually discussing any innovation in the matter of treatment the first rational thing to decide appears to be: Is the present treatment not entirely satisfactory or may better results be expected by a change? Rather than even presume to answer this let us survey the comments of some outstanding authorities in this particular field.

Halsted, in discussing breast cancer, says: "Notwithstanding the present day extensive operation, death from metastasis occurred in 23.4 per cent of the cases even where the axilla was microscopically negative."

Bloodgood emphatically states: "The incomplete operation hastens death."

Deaver expresses his general dissatisfaction with operation of a palliative nature, since in certain cases the disease has been excited to greater activity by the incomplete operation, and the life of the patient considerably shortened.

Greenough states that: "When the axillary glands are palpably involved only 12 per cent are cured by operation alone," but, he adds, "with proper raying this may be increased to 20 per cent."

Finister asserts that when the axillary glands are involved the number of final cures by surgery alone is 4.3 per cent and this latter figure Ewing confirms and claims that 4.3 per cent represents the average success by surgery unaided. This, then, must be interpreted to mean that a woman suffering with cancer of the breast has actually less than one chance in twenty of a cure, depending on surgery alone.

This, therefore, makes it appear that something better is desirable, for we

[1]Read at the Mid-annual Meeting of the Radiological Society of North America, San Francisco, June 22, 23, 1923.

cannot be satisfied with one success to nineteen failures in a condition unfortunately so prevalent as mammary malignancy. It is true that spectacular advances have been made in medicine, but in the fight against malignancy we have been disappointed, and no one would welcome a betterment of to-day's statistics with greater satisfaction than would the surgeon.

In the treatment of cancer there is but one method at the present time that offers promise of anything even so good as surgery, and that is the proper and intelligent application of radiotherapy. While scores of other methods have been tried, these two dominate the field to-day. But even though the actual achievements of radiotherapy are extremely gratifying and the newer advances even more so, yet here too the results leave much to be desired. To-day the literature is literally teeming with reports of failures, and no wonder! There is no branch of medicine where so much empiricism, guess-work, mimicry and actual downright charlatanism occur as in the so-called medical application of radium and X-rays. Much of the work is being attempted by men whose only qualification is their having access to some sort of an equipment and in many instances positive harm rather than good results. Yet despite all this the results in legitimate and scientific hands are such that Ewing comes out flatly with the statement, in discussing the treatment of malignancy by radiotherapy, that "it is the first rational treatment of cancer ever devised." This from an unbiased authority like Ewing demands attention and serious reflection. However, it is not only the pathologist who recognizes the value of the method, because to-day it is the custom in all well conducted institutions to add a series of rayings to the operation, as the surgeon has learned by experience that his results are better with this association. But one may well ask, "Is the radiation therapy being properly and intelligently handled and is the patient getting the maximum benefit from this method?" The answer to this is *positively and emphatically no.* The reason is also apparent. Just think for a minute what results one would expect in surgery if the operator received his entire instruction and training from the instrument-salesman. Try to imagine such a state of affairs. Yet despite the absurdity of such a thing there are cold, calculating, scientific men, otherwise ethical and intelligent, entrusting their diagnosis and treatments to technicians with no fundamental knowledge of the method other than that gathered from travelling instrument-salesmen. Nevertheless medical men all over this country are not only soliciting the opinions of unqualified laymen but are actually being dictated to by them, and, what is even worse, are, without hesitation, voicing their opinion of a method from their own observations which have been limited to this class of work.

The general consensus of opinion is that radiotherapy is an invaluable associate of surgery but it seems that by far the greater amount of raying is done after the operation rather than before. Frankly I must confess that I cannot understand this nor has any reasonable explanation ever been submitted so far, at least, as I know. It seems so obvious from the several viewpoints that this is not rational. The time to lock the stable door is while the horse is still there, and the time to apply the X-rays and radium is before the cancer cells have become disseminated. If the method has any virtue, why not use it before the lymphatics are opened into and before the blood stream has transported to distant organs detached tumor cells, each a potential new-growth? A still more important reason is, as will be shown later, the effect of the raying on the malignant cell it-

self in releasing an enzyme that is of definite value in the defense of the organism, and if the raying is done after all malignant tissue is removed the distinct advantage of this antibody is lost.

A most illuminating experiment was carried out in Germany a few years ago to determine the relative value of the two methods of treating carcinoma of the breast. Three groups each of fifty cases were gathered. The patients were relegated to the different groups exactly as they appeared. All were clinically mammary carcinoma. The cases in Group 1 were operated on, the particular operation being that deemed best suited to the individual case. The cases in Group 2 were treated by radium and X-rays, while the cases in Group 3 were given no active treatment at all to the breast condition. The astounding result of the experiment was that the cases in Group 3 had an average life which was longer than the group operated upon and the radiated group on the average outlived the other two. This is significant. Yet an observation of this kind and the daily observations of any one seeing many of these cases must impress him with the fact that the treatment of this condition is not so satisfactory as is generally desired, or, as Lee puts it, the results are not so good as is generally believed.

In breast conditions particularly there are a number of reasons for this. The chief one is the time at which the patient presents herself to her physician, often months after the discovery of the mass, and consequently at a time when the trouble is no longer a local tumor but a constitutional disease. The fact that the breast is supplied with one of the richest lymphatic systems of any organ in the body allows for an early extension and dissemination. This is aided by much unnecessary handling of the breast by the patient, her friends and her physician. The writer was rather impressed by the fact that at the Memorial Hospital only one visitor is allowed to examine a case, as Lee points out, and rightly so, that undue manipulation is not to the patient's best interest. Still another reason why results are not what could be desired is the fact that surgical removal is not always complete. But this is not of necessity a reflection on either the technique or the ability of the surgeon, because not only is it difficult but humanly impossible for him to be sure. Time and time again it has been shown that when one group of glands are palpably involved the neighboring glands and lymphatics are microscopically malignant despite the fact that there is no macroscopic evidence of their involvement. Why, then, demand from the surgeon what is unfair and unreasonable to expect? To be absolutely certain would mean a dissection so radical and so extensive that he would be literally taking the patient away from the tumor rather than the tumor from the patient. Yet it might be mentioned here that Gaylord has found that of the specimens sent to the New York State Institute for examination, having been removed as being cancer of the breast, only 28 per cent show to be malignant microscopically. So, therefore, it would appear that the surgeon is taking no chances about questionable cases.

There is another aspect of the question to be considered: Just what was the cause of the original malignancy? Is it not reasonable to suppose that the very presence of a cancer should be construed to mean an inherent weakness or predisposition on the part of the patient and then, allowing that the mass has been removed *in toto,* does it follow that the precipitating cause of the malignancy has been eliminated? So, therefore, the presence of a so-called "recurrence" may not be a reflection on the operation as having been incomplete but may mean a persistence of the condition that allowed of the de-

velopment of the original mass. So then one might even regard the treatment of the mass by removal, the treatment of a symptom only and not the actual treatment of the "disease." The apparent cures that do result may be accounted for by the fact that the defensive forces are relieved of some of their burden, but what appears more logical is the production of a state of affairs where malignancy cannot exist. The serious problem is: Just how can such a condition be produced?

Many workers have attempted this problem and though they have toiled for years no practical and dependable method has yet been achieved. The observations of Musser and Edsall in studying the changes that occur in the lung during resolution showed that there was developed a lysin or enzyme which resulted in a digestion of the inflammatory exudate. This substance was at first considered to be of bacterial origin but later it was shown to be a response of the body tissues. Edsall and Pemberton then demonstrated that the body cells liberate an enzyme after exposure to X-rays or gamma-rays and that this enzyme circulating in the tissues was responsible for some of the remote effects we have observed as due to radiation. As is well known a pure culture of micro-organisms can withstand without apparent effect a heavy dose of raying, yet the same organisms when infecting normal tissues are destroyed after raying. Obviously not due to the direct effects of the rays but, instead, due to the effect of a bactericidal something produced by the normal tissues under stimulation of X-rays. This and scores of other observations allow of the conclusion that normal and pathological cells under radiation stimulation release an enzyme which like others of this family eludes analysis, yet whose presence is conclusively demonstrated by clinical phenomena. So, therefore, it did not seem unreasonable to suppose or expect some results from investigations pushed along this line.

Bashford, Murray, Cramer, and Russel had already shown that a certain degree of temporary immunity could be conferred on animals by the injection of tumor material into them, but of course with the tremendous risk of starting new tumors at the site of injection. Even as far back as 1895 Hericourt and Richet had made attempts along this line and since then many investigators have delved into the problem. Bashford, Murray and Cramer showed that the injection of blood corpuscles into mice produced a temporary immunity against malignancy, while other workers were able to obtain similar results with various cellular tissues, but the results were not lasting. The immunity which did follow was highest at the end of the second week, then rapidly disappeared. Haaland demonstrated that the mechanical disintegration of the tumor cells resulted in a destruction of the ability they otherwise seemed to possess of conferring immunity. Other workers tried treatment by heat and by chemicals but without success, so that little chance of anything of a practical nature seemed likely because, if the tumor cells were injected without treatment of any kind the risk was too great, while every form of treatment so far tried vitiated the immunizing effect. It was not until 1910 that Contamin, working in France, showed that he could obtain immunity in mice by injecting into them tumor tissue which had been subjected to treatment by X-rays. He discovered that his dose must be very exact, for if it was *under* the injection set up new growths, while if *too much* treatment was given the cancer cells no immunity would result.

The work was taken up by Wedd, Morson, and Russ and they, too, were able to produce mice that were immune

to the injection of untreated carcinoma after inoculation with irradiated tissue. Later Chambers, Scott, and Russ carried the work still farther and produced mice that were permanently immune to any further injections of malignant tissue. Having secured a method of producing immunity they attempted to determine the degree produced by varying amounts of the injected irradiated material. Doses ranging from 0.003 c.cm. to 0.2 c.cm. of the irradiated material were injected into 80 rats, using Jensen rat sarcoma. It was found that very little difference was noticeable though it seemed the better results were obtained from the larger amounts. Then an attempt was made to find out at what time following the injection of rayed material, the immunity was greatest. It was found that at eight weeks the effects seemed more marked than at an earlier period, though here again very little difference was observed between the batches tested at one, two, four, six, and eight weeks.

Altogether they were able to secure immunity against four different types of malignant cells. So far, however, most of the work was done by first injecting normal animals with the rayed tissue then later testing their immunity to ordinary tumor material. Of course all these experiments were checked by suitable controls. Next, therefore, an attempt was made to determine the response produced by the injection of the irradiated tissue into an animal with an already established tumor. For this purpose a series of rats were inoculated with a slow-growing sarcoma, then eight weeks later when the tumors were easily apparent they were divided into two groups. One group were given an injection of freshly irradiated sarcoma and of these 87 per cent showed a regression of the growth to less than half that of the controls and in the greater majority of the cases the established tumor disappeared.

Another experiment was tried five days after injecting both axillæ with Jensen rat sarcoma (a very rapidly growing type). Half the batch were given a lethal dose of beta and gamma radiation to one axilla, the opposite side receiving a negligible dose, yet the tumors in this untreated side showed obvious reduction to less than one-half the size of the controls. It was found that a full lethal dose must be delivered else no reduction occurred in the tumor of the untreated side. Obviously this remote effect must be due to some systemic effect and it would seem probable that the disintegrating cells receiving the full lethal dose liberated some antibody which resulted in a definite reduction of distant growths.

An attempt to try to isolate the active principle causing these results was fruitless. Many methods were tried and discarded, even normal saline as a solvent appearing to destroy the effect. Chemicals and desiccation were tried and discarded; the substance, whatever it is, is not a stable one and will not withstand heat, chemicals, or drying. Obviously then the place to generate this substance is within the patient's own tissues either by pre-operative raying or the injection of treated material according to this method.

In May, 1920, Russ, Kellock, and Helen Chambers extended these investigations to the treatment of patients at the Middlesex Hospital in London and found that the same principles were applicable. It was found possible to inject carcinomatous tissue treated in this way without producing any new-growths at the site of injection, but even more gratifying was the fact that in some of the cases a resolution of the malignancy occurred. At first only cases that were hopelessly inoperable were attempted and subjected to this procedure but later, as results seemed to justify it, earlier cases were attempted. The writer has tried this

method in a very limited number of cases but with what so far appears to be a decided success. Some of the cases Russ attempted were so far advanced that really no results could be reasonably expected from any form of treatment, yet he did report that of five cases of carcinoma of the breast treated between November, 1920, and June, 1921, all were in good health and free from any evidence of recurrence when last seen. In four of the cases the primary growth only was removed, leaving obviously involved axillary glands.

In the very limited experience of the writer in applying this method three cases only have been attempted and while the number is small and the time elapsed too short yet the observations of others have been sufficiently confirmed to arouse my intense interest. Two of my own cases were breast carcinoma, one a spheroidal-celled and one a duct carcinoma, the other was a case of round-cell sarcoma of the neck. All showed glandular involvement and the glands were not disturbed in any of them. All have shown an apparent relief from obvious symptoms. But let it be distinctly understood that this is not an attempt to report a record of three cases of a radical departure like this. What work I have done is merely to obtain first-hand knowledge of the method and so confirm the reports of others. Russ and his associates have now treated a fairly large number and with characteristic British conservatism are slow at rushing into print until they are absolutely certain of their work.

In the description of his technique Russ makes use of a term "Rad" which is not well known in this country but which he uses to define that amount of radiation under fixed conditions necessary to prevent the growth of a Jensen rat sarcoma when introduced into normal animals. This is difficult to translate into the ordinary formula used here so that is was necessary to do some little experimental work of my own to determine it, and the technique that was used in my own cases was using a tube backing 35 cm. between blunt points passing 5 ma. of current at a distance of 25 cm. from the tumor tissue and an exposure time of 32 minutes using a filter of 1 mm. of Al. plus 1 mm. of glass. This I feel is probably a heavier dose than that used by Russ and described as a Rad, but it appeared to be safe as judged by three cases.

The *modus operandi* is that the primary mass if easily accessible, or a portion of it, is removed under strict surgical aseptic conditions. Then the tumor is carefully dissected free from all fat and adventitious connective tissue. It is then ground very fine, spread out in a thin layer about 3 cm. thick in a sterile Petri dish. This is now given two Rads, that is, 32 minutes, on one side then turned upside down and given another 32 minutes on the opposite side. Meanwhile the wound is being closed without any attempt to do a dissection of the involved glands. When this is done two linear incisions are made into the rectus muscles. A pair of Spencer-Wells forceps are introduced into the muscle and opened, then withdrawn. A large drainage tube is introduced into each rectus, the skin sutures inserted and left untied. A sterile dressing is applied and the patient sent back to her bed. Before she has fully recovered from the anæsthetic the tumor material has been prepared as described and is introduced through the rubber tubes which are now withdrawn and the skin sutures tied, the wound sealed and left untouched.

Following this there are no untoward symptoms. One patient did develop a temporary œdema around the abdominal wound but this disappeared in 48 hours; the others showed no evident reaction other than what

would be expected from an ordinary skin incision of this nature. There was a very distinct reaction around the glands in two of the cases. They became sore, œdematous and evidently swollen on the tenth and twelfth days, respectively. This, too, was a transient thing, however, for on the fourteenth day they were both subsiding and at the end of three weeks there was an evident reduction in all three cases, and at this date they all appear to be relieved from their metastatic involvement. One of the cases was untreated except as described; two were treated by pre-operative radiation, and this I personally feel is still desirable because of the reasons already set forth.

This then, gentlemen, is the message that I bring, not in any way meant to be either original or conclusive but merely the reiteration of the work of others with a line of attack that appeals to me as being very rational and following already established principles. No one is more fully aware of the absurdity of an early report than the writer, but the importance of this as it appeals to me would seem to justify an early report to a body of this nature with the expectation that it may be taken up by some really qualified investigators and so the actual value and use of this method as well as its limitations and dangers may be early made known.

CONCLUSIONS

The results of the present treatment of malignancy, particularly carcinoma of the breast, is not all that could be expected.

The association of moderate surgery following a properly calculated and delivered dose of radiotherapy is productive of better results than without the raying.

The practice of operating and then some time, often months, later giving the patient a series of irradiations is not sound. The time to administer the raying is before and immediately after the operation, if an operation is considered necessary.

Some of the remote effects of raying are to be explained in the formation of an enzyme liberated from living tissues and therefore the intensive raying of a tumor mass may and sometimes does cause the resolution of a distant mass.

The recurrence of malignancy is not necessarily an indication of poor surgery but may mean an inherent predisposition on the part of the patient.

The fact that an increase in the resistance to malignancy may be possible would seem to indicate that its properly guarded use would be conducive to better results.

Through the irradiation of the individual's own cancer and the re-introduction of this treated material, a resolution of the metastasis may be induced in some cases without setting up a new growth.

The dose applied to the tissue to be re-introduced should be exactly calculated, as too small a dose will result in the starting of new tumors while an overdose will destroy the immunizing effect of the treated cancer tissue.

The treatment should not be attempted without the co-operation of a surgeon pathologist and a trained radiologist who has the necessary instruments of precision available and who is conversant with their use.

The method is potentially as dangerous as it is promising but it is based on already established principles as used every day in vaccine therapy.

The association of infection or antiseptic chemicals vitiates the attempt.

The method is new, this report is merely tentative, but the results would seem to justify further investigation and it is sincerely hoped that this effort will result in the bringing of this method to the attention of investigators so that we may without delay be in a position to realize the full value and the limitations of the method.

RADIATION DOSAGE: STANDARDIZATION VERSUS INDIVIDUAL ADAPTATION[1]

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SOME years ago a compound was heralded as a cure for syphilis. A remedy that would, in a few doses, kill all the spirochetes, following which, of course, the host would cease to have syphilis. It was soon found that while salvarsan was one of the best, if not the best, agent in treating the disease, it far from sterilized the patient of his infection. Today we hear little of the necessity of placing the patient in jeopardy of his life from enormous doses in the hope of eradicating the spirochete over night. It is now one technique for early syphilis, another for neurosyphilis, etc. And we also hear of the patient's reaction, whether he is able to stand large doses at long intervals or whether, in a particular case, it is not better to give small ones frequently; in each instance basing treatment on the daily progress of the case. In short, to individualize.

For many years superficial cancers have been successfully treated by two methods of cauterization, by heat—the actual cautery, surgical-diathermy, fulguration—or by radiation and bombardment with electrons. By each method the malignant cells were destroyed along with a proportion of neighboring normal cells and the defect was repaired by tissues which were beyond the range of the destructive agent. In the use of radiation and electron bombardment it was observed that in the majority of instances the malignant cells could be made to undergo a change resulting in their replacement by normal tissue without necrosis taking place—in short, a metamorphosis without cellular death. We soon learned that it was unnecessary in certain cases, to produce cauterization, *i. e.*, to kill the cancer cells with the attending long period for healing, in order to rid the patient of his cancer.

In treating deep-seated malignancies it was impossible to place a cauterizing or lethal dose into the tumor without injuring the skin beyond repair. Unfortunately in the attempt to do so many a victim to misplaced zeal has had a radiation skin burn added to his burden of an internal malignancy. Now physicists and engineers have given us equipment with which we may place any quantity and almost any quality of radiation we may desire into any part of the body at any depth. At first this was heralded as the great cure for cancer. If we can kill the cancer cells in the skin by a sufficiently large dose, we can kill them at a depth by putting that dose into them. It reminds one of the hopes raised by the early report of the use of salvarsan. The amount of radiation required to kill cancer cells is stated to be so many erythema doses—we all know what a variable thing that is—so many electrostatic units, etc. We are told that we must put this amount of radiation into all parts of the tumor in the shortest possible time in order to obtain the desired lethal effect on the tumor cells. We are warned that serious results to the patient as well as to the tumor may result from these doses but that they are a necessary evil just as shock, hæmorrhage, etc., may occur in surgical operations and that, therefore, the risk is justified. Probably the question most frequently asked among radiologists is, "What is your cancer dose? Do you use 450, 700, or 900 milmin. and do you give it in one, five, or ten days?" The questions nearly always relate to the physical factors used to produce the hoped-for cure, the

[1]Read before the Radiological Society of North America at the Mid-annual Meeting, San Francisco, June, 1923.

amount required to actually kill the cancer. Can we hope to kill cancer with a definite quantity and quality of radiation, just as we hoped to kill all the spirochetes in the patients' tissues by definite dosage of 606? Are we not leaving out of consideration multiple factors of body reactions which play a major role in the ultimate cure of any condition which may not actually be cut out of the sufferer's anatomy?

Ewing (1) emphasizes the role of both body and tissue reactions in radiation effects on tumors. He states that in general the different tissues maintain within certain limits a uniform reaction to radiation, but anything like a uniform standard reaction of the tissues does not exist. The different tissues behave in a rather variable manner toward radiation and this behavior may be greatly altered by previous structural changes and other pathological conditions. These considerations are especially pertinent when they concern the state of the tissues immediately adjacent to a tumor that is to be radiated, since upon the reaction of such adjacent tissues the result of the radiation will largely depend. The therapeutic goal varies with many complicating circumstances, and each case becomes a study in itself. The idea that anything approaching a uniform dosage can ever be established for all the various forms of carcinoma, or all the varieties of sarcoma, can be entertained only by those who deal with a few common types of cancer which they imperfectly observe, or by those whose work is confined to the experimental cancer laboratory. This attempt to substitute physics for biology and medicine can only prove an obstacle in the way of sound progress in radiotherapy. The conception of a standard dosage seems to emanate mainly from the notion that radiation cures cancer by killing cancer cells. The idea is an inheritance of the old surgical point of view, that the cancer must be extirpated, root and branch. There is no cancer cure without a tissue reaction and under some circumstances when this reaction fails, no amount of radiation succeeds in killing the tumor cells. He has seen tissue after heavy radiation where necrotic stroma tissue supported well stained and apparently viable tumor cells. He believes that the most detailed knowledge we possess indicates clearly that the curative action is not the result of a direct effect exclusively upon the tumor cells, but involves especially a peculiar reaction of the normal or invaded tissues. A simple morphological interpretation reveals the highly important fact that in treating cancer by physical agents we are not merely killing cancer cells, in the sense of the physicist, nor extirpating them entirely, according to the surgeon's plan, but rather are calling upon Nature's forces to accomplish the cure.

Russ, Chambers, and Scott (2) found that prolonged exposure of animals (rats) to radiation resulted in severe wasting and death; with a reduction in the exposure, a growing animal will retain its health, but with a diminished rate of increase of body weight. As the dose of radiation becomes less, a stage is reached when the rate of increase of body weight exceeds that of the normal animal; and, when the animal is given these very small doses it is found to develop a state of increased resistance to an implanted tumor. They also found that if small repeated general daily radiations were given to the inoculated animals, with the tumor area protected, there was a slowing-up of the tumor growth but that there was much less retardation if the tumor received these small doses at the same time. They believe that there is ample evidence that large generalized doses of radiation lower the normal resistance to tumor growth but that this result is reversed when small generalized doses are given at frequent intervals while

the tumor is left unrayed. If the size of these daily doses were varied, it was found that the more prolonged did not give the higher immunity.

Murphy and Morton (3), Mottram and Russ (4) and Prime (5) have shown that after very large doses of X-rays an immune animal becomes temporarily susceptible to carcinoma and sarcoma inoculations.

Chambers, Scott, and Russ (6) found that a single rather large dose of X-rays increased the susceptibility of the animals to inoculation with spontaneous rat carcinoma.

We have all observed small nodules of lympho-sarcoma in unradiated parts of the body regress or disappear after the larger masses had been irradiated.

If, then, it is true, and the evidence, if not conclusive, is very strong—

1. That malignant cells are not killed in the ordinary sense by radiation;

2. That an optimum tissue reaction to radiation is necessary to obtain a cure as well as a detrimental reaction to radiation in the tumor cells themselves, and that this reaction of normal tissue is brought about by small doses, while the desired change in tumor cells follows larger ones;

3. That light radiation renders the host more resistant to tumor growth while heavy radiation makes him more susceptible;

4. That the optimum radiation for any given tumor depends, not only on the kind of tumor cell, but on multiple factors involving the physical condition of the host, *i. e.,* the ability of his tissues to produce the desired reaction—we must stop the search for the carcinoma dose as expressed in physical factors of wave length and intensity alone. We must first standardize our physical factors or allow the physicists and engineers to standardize them for us so that we may repeat any desired condition of radiation at will and then apply these known factors in varying degrees to each individual as our experience may dictate. We must stop reporting cases of carcinoma as receiving so many units of radiation with conclusions that N per cent will be cured if this dosage is used and that if the engineers will give us apparatus more powerful we will cure 2N per cent of all cases. We must record the clinical observations, the bodily reactions, in every case. This has been done on comparatively small groups only and too frequently without correlation with the physical factors of quantity and quality of the radiation used. Let us think in terms of the body as a whole as well as in terms of the tumor in question. Perhaps, when sufficient data has accumulated we will know why the same kind of tumor under the same dosage will melt away in one individual and be almost unaffected or progress more rapidly in another. Perhaps then we will find that by adapting the dose to the individual all tumors of a given type will disappear and even some that are considered hopeless today may be those most easily cured tomorrow. We must remember that the cure of cancer by radiation is not the problem of the radiologist alone. The problem is too large and involves too many factors. We must turn for help, not only to the physicist but to the internist, the endocrinologist, the metabolist, the pathologist, and above all to the physiologist. These have all learned through bitter experience that only broad principles apply to every case and that in each problem factors peculiar to the individual must be taken into account before the final interpretation can be made.

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THE TREATMENT OF PRIMARY AND LATENT INJURIES OF THE SKIN FROM RADIUM AND X-RAYS[1]

By HENRY SCHMITZ, M.D., CHICAGO

THE application of rays may cause immediate and latent changes in the exposed skin area. These injuries have been termed radium or X-ray burns and ulcers. The observations related in this paper were made chiefly in diseases of the pelvis subjected to radiation treatment and are equally applicable to similar conditions in other regions of the body.

Skin exposed to radium and X-rays reacts in the same manner as it does to sun or light rays. The reaction to rays of the different areas of the same individual varies somewhat. The skin of the back is more sensitive than that of the anterior surface of the body—presumably due to pressure and excessive moisture, as perspiration, while in the recumbent position. The deep folds of the skin show a greater sensitiveness due to the frequent presence of moisture and the predominance of erythema and eczema in such areas. Thus after X-ray treatment we frequently see excoriations and ulcerations in the ano-genital fold and the lower traverse crease in the anterior abdominal wall in corpulent women, while the skin of the surrounding portions of the radiation field evidences only a reddening with subsequent browning. Laparotomy scars, also, may show such a predisposition to radiation injury. Certain substances applied to the skin for various purposes render it very sensitive to radiations, as iodine, solutions of lysol, mercurial ointments, vaseline and so forth. Long-continued pressure from corset stays acts likewise. Certain diseases, as lues, nephritis, eczema, trichinosis, and hyperthyroidism render the skin peculiarly susceptible to injuries from rays. It is well known that the skin of titian people is very sensitive to rays—sometimes as much as one-third to one-half more than the skin of average people.

A weak but long-continued action of the rays causes a tanning of the skin. The discoloration is usually accompanied by a slight scaling of the epidermis appearing about eight to ten days after radiation. The tanning of the skin may persist for months or years. It is more intense the softer the rays are. A heavily filtered radiation is followed by a less intense tanning. A 100 per cent erythema skin dose will cause these superficial and temporary changes. Restitution to normal is complete.

If the dose of rays applied is larger, then the skin will show within fourteen to twenty-one days an inflammatory reddening and destruction of the superficial layers of the epidermis. A more or less severe itching is present. Within six to eight weeks the erythema will disappear; the skin becomes tanned deeply and epilation is almost complete. The tan may peal off within nine to twelve months leaving a normal white skin behind. Quite infrequently telangiectasis appears in the center of the field. Most of the hair will regenerate. A 130 per cent E.S.D. usually causes these burns of the first degree. Should the same radiation dose be repeated within six to eight months then the epilation may become permanent. A persistent œdema and induration of the epidermis, the cutis, and the subcutaneous fat may appear. These may last for years.

Should a still larger radiation dose have been applied, for instance 130 to 150 per cent E.S.D., then a burn of the second degree will be caused. Vesiculation appears with the erythema. The blistering is strongest in the center of the radiation field. The blisters rupture

[1]Read before the Radiological Society of North America at the Mid-annual Meeting, San Francisco, June, 1923.

leaving a more or less deep ulceration behind. The latter becomes covered with a crust. Healing is rather protracted. It will be completed under favorable circumstances within two to three months. The area is a clear white, devoid of any elasticity, and telangiectases will form within a short time. These changes are permanent.

If the radiation dose applied is about 150 to 200 per cent of an E.S.D., then a burn of the third degree results. More or less deep necrosis is seen, sloughing occurs and the tendency to heal is very slight. Months may pass by before healing is complete. Often a secondary or latent ulceration occurs within a year or two—the so-called X-ray or radium ulcer.

Radium applied with the same intensities will cause identically the same signs. There does not seem to be any difference in the healing comparing radium and heavily filtered high voltage X-rays.

Repeated applications of small doses of rays distributed over long periods of time are much more apt to cause severe intractable injuries of the skin than one dose of highly filtered X-rays or gamma rays. Roentgen and radium cancer also will not occur after a single, even large, dose, though frequently repeated exposures often terminate in malignancy.

The treatment for the erythema and superficial loss of the epidermis is the application of Dodd's lotion.

℞	Zinci Oxidi	16.0
	Glycerini	4.0
	Phenolis	2.0
	Aquæ Calcis	175.0

M. et S.: Apply with cotton every morning and evening.

The treatment of the second and third degree primary burns consists in warm baths, moist dressings or sodium bicarbonate, the actinic rays, the ultra-violet rays, exposure to sunlight, paraffin gauze dressing, Dodd's lotion, ointments of organic fats containing digestive ferments, zymol ointment, 25 per cent solutions of argyrol, and so forth. The ulcerations frequently resist all treatment. We then should excise the

Fig. 1. Latent X-ray ulcer appearing about 18 months after one application of a 100 per cent E.S.D. of X-rays filtered with 0.5 mm. copper + 1 mm. Al., a f. s. d. of 65 cm., and 130 K. V. crest.

ulcer with the electric cautery or surgical diathermy. As soon as healthy granulations appear which show a tendency to persist and are not covered with a grayish pseudo-membrane, then we may cover the raw surfaces with skin gratts or with transplantation of pedicled skin flaps.

Latent injuries of the skin are the result of too large or too frequently repeated applications of radium and X-rays, as mentioned before. Such latent changes are seen within one to three years following the primary injury and consist of an induration and swelling of the entire cuticle and especially the subcutaneous fat. The underlying fascia and muscles are frequently included in this process. The structures appear boardlike. The skin is distinctly ele-

vated over the level of the surrounding unaffected skin. Soon the tissues begin to break down in the center of the area. An ulceration appears which will slowly spread laterally as well as inwardly.

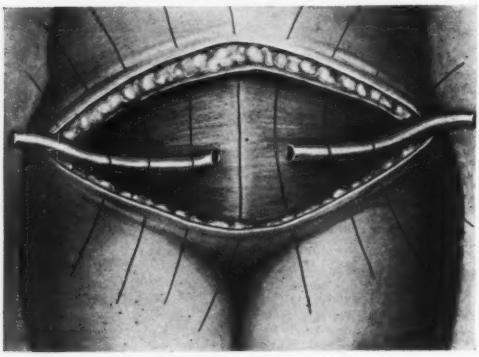

Fig. 2. Excision and repair of ulcer seen in Fig. 1.

Such changes in the skin are frequently seen in laparotomy scars, in the deep folds of the skin as in the anterior abdominal wall and the anal fold, especially if the skin is continuously moist or erythematous.

These changes cause a feeling of tenseness and a sensation of continued drawing. The most prominent symptom, however, is an excruciating, continuous, sharp pain.

The microscopic examination of a beginning latent radiation ulcer shows an inflammatory round-cell infiltration immediately surrounding the area of ulceration. The damaged tissue reveals a degeneration of the blood vessels with a thickening of the blood-vessel wall which at times obliterates the lumen. The endothelial cells apparently do not regenerate. Necrosis is the final result.

The principles of treatment consist in the removal of all pressure and irritation. Ointments of digestive ferments may be applied. Sunlight and actinic rays, also high frequency currents are especially useful for the relief of pain. Constant immersion in water causes an improved transmission of blood through the diseased part. The result is that some particles of tissue are saved because of a regeneration and that a line of demarcation forms much sooner, whereby the necrotic tissue is separated. Applications of hot chamomile dressings or stupes of normal saline solution have also been used to attain an early demarcation. Wintz states that such ulcers and indurations will, after a year or two, evince a tendency to heal if kept free from all pressure and external irritations. According to Bevan the basic principle involved in the treatment of X-ray burns is the necessity of removing the injured tissue, and then by skin grafting or plastic operation or granulation obtain complete repair. Excision offers immediate relief from the excruciating pain.

Should the ulcer resist the various methods of treatment and demarcation be complete, then we excise the X-ray induration and ulcer if they involve the skin only. Should the skin be firmly fixed to the fascia and muscles of the anterior abdominal wall then excision is contra-indicated, as we cannot remove these tissues without causing permanent invalidism. The incision must be made in the healthy skin surrounding the indurated area.

The illustrations in Figures 1 to 4 show the procedure. The first patient had a *"Hangebauch,"* and was very obese. One and a half years after cessation of the usual treatment which had not caused any primary reactions she developed an ulceration with induration in the deep portion of the skinfold. It did not spread but resisted all treatment. The patient complained of an excruciating sensitiveness in the ulcer. A lipectomy was performed, as seen in Figure 2. Healing occurred by first intention.

In another patient a second X-ray treatment of a 100 per cent E.S.D. was

inadvertently applied within three months after the first exposure. No immediate burns occurred. Two years later an indolent ulceration of a progressive character within an area of in-

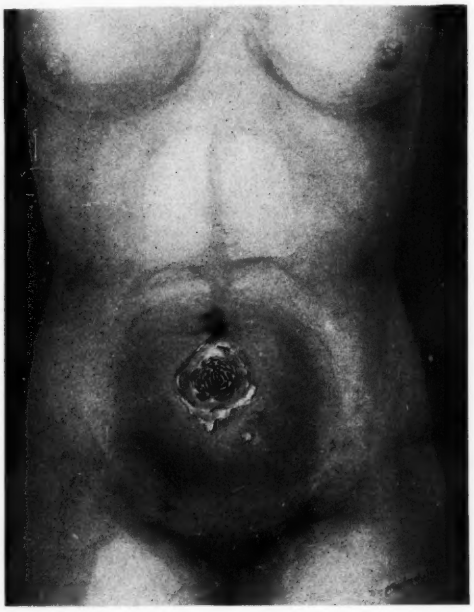

Fig. 3. Latent X-ray ulcer and induration seen about two years after two applications of 100 per cent E.S.D. X-rays had been given with an interval of three months between applications.

duration appeared. The latter was confined to the radiation field, which was round, had a diameter of 15 cm. and was fixed to the underlying tissues (See Fig. 3). The ulcer was resistant to all treatment. One year later we excised the skin and underlying fat down to the fascia. The ulcer extended through the skin only. An incision was made in the median line. The fasciæ and muscles were dark brownish yellow; the peritoneum appeared to be normal. The pelvic organs were negative. The adnexa were free, the uterus movable, small, and hard. The parametria were of a normal consistency. The regional lymphnodes were negative. The serous surface of the bowels also did not show any changes. Adhesions were nowhere found. A plastic repair with transplanted pedicled flaps of skin was done. However, the skin covering the indurated tissue became necrotic and sloughed. Healthy granulations soon covered the entire area. They were at first covered with a grayish pseudo-membrane. Soon epithelization took place which advanced rapidly to an almost complete healing. (See Figs. 3 and 4.)

In conclusion we may state that in X-ray and radium therapy we must avoid (1) over-dosation, (2) too early re-applications of a full skin dose if otherwise the technique is perfect. We

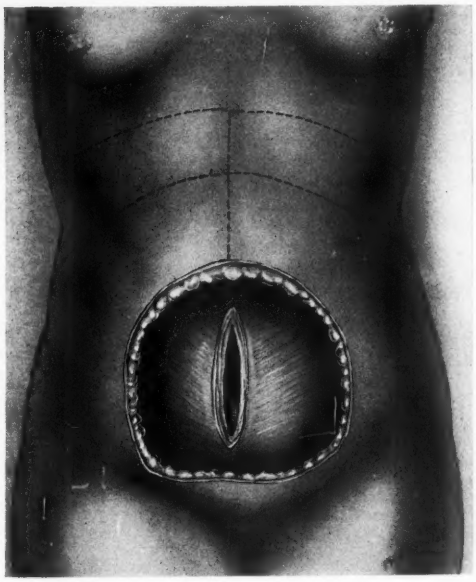

Fig. 4. Excision of X-ray tumor seen in Figure 3, one year later, after unsuccessful attempts at local treatments. Healing by granulation.

must know the fluctuation in the X-ray intensity by repeated measurements of

the output of tube and transformer, by observing proper filtration, correct focal skin distance and prevention of overlapping of radiation fields. We, also, should not apply radiations if the patient has already been treated at another clinic unless we have obtained an exact report of the radiation treatment employed.

If early or late injuries result from the application of rays we should treat them expectantly and remove all sources of irritation from the skin, as pressure and irritating medicaments. Should the diseased area of the skin be freely movable over the underlying fascia and muscles and not show any tendency to regeneration, then an excision with subsequent skin grafting or plastic graft may be performed. If the deeper structures are involved, then watchful waiting appears to be the best method of treatment unless such areas are located in regions of the body where a complete excision would not be followed by a permanent defect or weakening in the anatomic structures.

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STUDIES OF THE EFFECT OF X-RAYS ON GLANDULAR ACTIVITY

III. THE EFFECT OF X-RAYS ON GASTRIC SECRETION[1]

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IN a previous communication (1) we have presented evidence showing that the secretion of the submaxillary gland in the dog cannot be stimulated by small doses of X-rays and that a dose of 110 K.V.M., 10 ma., 30 cm. f. s. d., 28 cm.[2] portal, 1 mm. Al. filter for 37 minutes is required to depress its secretory activity. This dosage amounts to two "dog erythema doses," or five "human erythema doses," since we have found that the dog's skin is from two and one-half to three times less sensitive than the skin of man.[2]

The submaxillary gland was selected as the first gland for our study because much is known concerning its physiology and because it lends itself so readily to experimentation. We have chosen the gastric glands as the second gland for study for the same reasons.

A review of the literature shows that no experimental work has been done on the effect of X-rays on gastric secretion. Regaud, Nogier and Lacassogne (2) working in 1912, report that the glands of the fundic portion of the stomach were found to have undergone complete atrophy in a dog which had been exposed to a total of 63 H. (3 doses of 9 H. with 2 mm. Al. filter, 1 dose of 14 H. with 3 mm. Al. filter, and 1 dose of 22 H. with 4 mm. Al. filter) given in five doses over a course of fifteen months. They made no observations on the gastric secretion of this dog.

There are several clinical reports, however, stating that X-ray has been used with beneficial therapeutic results in hyperacidity. Winternitz (3), in 1910, reported that radium even in relatively large doses in radioactive water (4000 mache-einheit, or 400,000 volt-abfalleinheiter) has no influence on gastric secretion. Bruegel (4), making observations on ninety cases, reports that the acidity of the gastric secretion is reduced when exposed to 16 to 20 H., using a filter of 3 mm. Al. and 1½ mm. of hard rubber and a 30 cm. focal skin distance. He administered 4-5 H. anteriorly and posteriorly over the stomach and then in fourteen days repeated the dose. He attempted to stimulate the gastric glands in cases of hypo- and anacidity by using stimulating doses of X-ray (he does not give the doses used) with negative results. Wilms (5) in a very brief report states that in certain cases of pylorospasm X-rays have a beneficial therapeutic effect, which he explains as due to the reduction of the acidity of the gastric secretion. Stephan (6) reports a case of achylia gastropancreation which on being irradiated with one-tenth of an erythema dose showed improvement in the pancreatic deficiency without any change in the achylia gastrica. Szego and Rother (7) state that they could influence gastric secretion only with a dose greater than an erythema dose and that when this was done they observed, first, a stimulation, followed by a depression of gastric secretion. Bryan and Dormody (8) report two cases in which they reduced the acidity of the gastric secretion approximately 40 per cent by irradiating the gastric area with four doses of X-ray, each dose consisting of 35 ma.-min., 80 K.V., and 33 mm. Al. filter, and 10 inches focal skin distance, administered

[1]Read at the Midyear Meeting of the Radiological Society of North America, Detroit, December, 1922. A preliminary report was made before the same society at St. Louis, May, 1922.

[2]Since making our observations Martin and Rogers (*Am. Journ. Roent.*, 1923, x, 11) have reported that the dog's skin is three times less sensitive than the skin of man. Our observations were made in the Fall of 1921, but were not reported.

in one case within a period of three weeks and in the other within a period of three months. This clinical evidence is open to criticism that proper controls were not made.

Although the evidence as presented in the literature is not satisfactory, it suggests that gastric secretion is decreased by rather intensive irradiation of the gastric area and that it is uninfluenced by small doses of X-ray.

METHODS

In our work the so-called Pavlov pouch dog has been used in which a portion of the stomach has been isolated

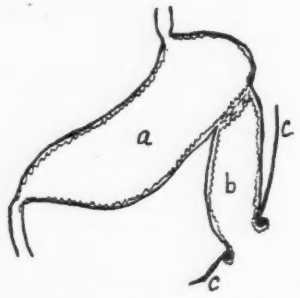

Fig. 1. Diagram of a Pavlov pouch, or accessory stomach, with nerve and blood supply intact. *a*, the main stomach; *b*, the Pavlov pouch; *c*, the abdominal wall.

with blood and nerve supply intact and opened to the outside so that the gastric juice can be collected and studied. (See diagram and picture.)

Two weeks, or longer, after the operation at which the pouch was made control experiments were started. The control experiments consisted of collecting the continuous secretion of the pouch for one or two hours and then feeding the animal a test meal and collecting the secretion hourly for four hours following the meal. The test meal consisted of 250 gm. of ground raw meat. The hourly secretions were measured for amount, titrated for free and total acidity, examined for peptic activity by the Mett's tube method and analyzed for concentration of chlorides. From ten to twenty control experiments were made to ascertain the normal physiological variation of the gastric secretion of the animals we were observing. After the series of control experiments the Pavlov pouch of the animals was exposed to varying doses of X-rays, the rays being so directed as to strike the pouch and overlying ab-

Fig. 2. Pavlov pouch dog prepared for collection of secretions.

dominal wall only. It was impossible, however, to exclude the spleen from the path of the X-rays, but we are certain the intestines were not included, except possibly by very peripheral and secondary rays, as we will show later in our paper. Following each exposure the animals were given a test meal and their secretion observed practically every other day for a prolonged period (three weeks to three months). That is, we allowed sufficient time for the X-rays to produce their effect before exposing the pouch to another dose of X-rays.

By these methods we have been able to study in six dogs the immediate and delayed effect of small and large doses of X-rays on the interdigestive secretion of gastric juice and on the gastric secretory response to a meal of meat.

It should be mentioned that the Pavlov pouch is located just beneath the abdominal wall in the upper left quadrant.

RESULTS

The interdigestive secretion of gastric juice varied in our dogs per hour from 0.5 c.c. to 2.0 c.c. in amount and from 0.02 per cent to 0.10 per cent in total acidity.

We have been unable to find a dose of X-rays, small or large, that would increase the amount or the acidity of the interdigestive secretion.

A large dose of X-rays, such as 110 K.V.M., 5 ma., 30 cm. f. s. d., 1 mm. Al. filter, 6 cm. dia. portal, for one hour, abolishes the interdigestive secretion ten to fourteen days later after exposure, nothing but mucus being secreted from the gastric mucosa. Biologically this dose amounts to from 160 to 170 per cent of a "dog's erythema dose" and 400 per cent of a "man's erythema dose."

We have not been able to find a dose of X-rays that will cause a hypersecretion of the stomach or that will increase the gastric secretory response to a meal. The smallest dose that we have used has been 60 K.V.M., 3 ma., 30 cm. f. s. d., 6 cm. portal, for 3 min. and no filter, which is approximately 30 per cent of an erythema dose of unfiltered X-rays for man and 12 per cent for the dog. We have also used doses that are equivalent to 50 and 75 and 100 per cent of an erythema dose for man without stimulating gastric secretion or rendering the gastric glands more sensitive to food stimulation.

Gastric secretion in response to a meal was abolished when the pouch was exposed to the following dose: 110 K. V.M., 5 ma., 30 cm. f. s. d., 1 mm. Al. filter, 6 cm. dia. portal, for one hour, which amounts to from 160 to 170 per cent of a "dog erythema dose." A second degree (shallow ulcer) was noticed seven to fourteen days after exposure and acid disappeared from the secretion ten days later. Free acid was absent from the secretion for three weeks. Six weeks after exposure the secretion had returned to normal acidity, but the amount was reduced by 50 per cent of the normal before exposure to X-rays. We have made such observations on six Pavlov pouch dogs.

This large dose of X-ray decreases the secretion of pepsin, but not to the same extent as the secretion of acid is decreased. The decrease in acid content appears from several days to a week prior to the decrease in pepsin. In two dogs a liquid secretion following the meal occurred, which resembled gastric juice in appearance, chloride and pepsin content, but contained little or no free acid.

The cloride content of the secretion is not appreciably altered.

In one dog only the lower, or outer, half of the pouch was exposed to X-rays. The non-irradiated portion continued to produce acid. The irradiated portion ceased to produce acid and pepsin, the superficial mucosa sloughed and at the center of the irradiated area two ulcers appeared, one of them perforating, the animal dying of peritonitis.

In the dogs that died, one dying of acute "roentgen cachexia," or that were killed ten to fourteen days following X-rays, petechial and small areas of ecchymotic hæmorrhages were found in the mucosa.

The histological changes that occur in gastric mucosa following X-rays are so interesting and important that we are reserving their report for a subsequent paper.

Two dogs that were kept for eight and ten weeks after they had received two "dog erythema doses" died of "chronic roentgen cachexia," gradually becoming more and more emaciated. These observations will be referred to again in a subsequent paper.

DISCUSSION

We want first to call attention to the fact that these results are due to the effect of irradiation of the stomach mucosa itself and not a referred or indirect effect, with the exception of the one animal that died of acute "roentgen cachexia." That this is true is amply demonstrated by our observations on the animal in which only a part of the pouch was irradiated and will again be demonstrated by our observations, to be reported in Part IV on "The Effect of Exposure of the Intestines to X-Rays on Gastric Secretion."

Fig. 3. Section of mucosa from the pouch 14 days after a 140 per cent of a "dog erythema dose" of X-rays, showing an ecchymosis. (Magnification 65 dia.)

That the depression of gastric secretion following large doses of X-rays is due to a general systemic effect is very probable, because it is well known that the gastric glands are easily depressed by nervous, systemic, and toxic factors. It was impossible to exclude the spleen in our animals, which was already markedly atrophied and microscopically showed marked fibrosis. But it has recently been shown by Inlow (9) that the removal of the spleen has no effect on gastric secretion. This observation does not preclude, however, the possibility that absorbed toxins from the atrophying spleen, the injured gastric mucosa of the pouch, and the skin burns were the etiological factors in depressing the gastric secretion in our experiments. We will again cite our evidence on the animal in which only a part of the pouch was exposed to X-rays which renders untenable the first two possibilities. The third possibility, that of the skin burn, is rendered untenable by an experiment to be reported in detail in Part IV, in which the mid-thoracic area of a Pavlov pouch dog was exposed to a "dog erythema dose" of X-rays, a skin burn 5 cm. in dia. resulting without any effect on gastric secretion. So we are certain that the effects that we observed

Fig. 4. A Pavlov pouch that had received two "dog's erythema doses" of X-rays, the first one 50 days and the second 21 days before death due to peritonitis secondary to a perforated ulcer of the pouch. *a*, the perforated ulcer; *b*, an ulcer, the base of which is muscular tissue. Good gastric juice was secreted by the upper or unexposed area of the pouch.

in our experiments were due to the direct effect of the X-rays on the gastric mucosa.

It is true that during the height of the depression of gastric secretion following the X-rays, the appetite of the animals was decreased. But the animals ate their test meal. This shows that there was a slight systemic effect, but not sufficient to account for our findings.

The genesis of the "gastric-juice-like" secretion containing no free acid is very interesting. At first we interpreted this finding as meaning that the mechanism for forming the acid of the secretion had been interfered with without affecting the mechanism responsible for secreting the fluid portion of the secretion. On further deliberation, we are inclined to interpret this finding as a transudate associated with the œdema and increased permeability of the capillaries that accompany the effect of X-rays on tissues in general. That the chloride content of the secretion is not appreciably altered, however, argues against this view. We are not ready to state which interpretation is correct, because this secretion was observed only after the animal was fed a meal.

Although our observations show that gastric secretion can be depressed by X-ray therapy, we are not convinced that it is a good therapeutic principle to treat cases of hypersecretion with X-rays. With the evidence that we have at the present time, we believe that permanent injury is done to the gastric glands by a dose of X-rays sufficient to depress secretion when directed into the stomach without inclusion of other organs, *e. g.,* the intestines. Would it not, then, be a much better therapeutic procedure to combat the cause of the hypersecretion, or if the cause is unascertainable, to use some inoffensive agent in neutralizing its effect?

From our evidence on the submaxillary and gastric glands we would say that the gastric gland in a dog is 40 per cent of a "dog erythema dose" more sensitive than the submaxillary gland. This is the result that would be anticipated in the light of the observations of Regaud, Nogier, and Lacassogne (2) and of Warren and Whipple (11). The first group of investigators observed that in their dogs which showed an atrophy of the gastric glands that the overlying mucous cells were not damaged and that the mucosa of the pyloric antrum, which secretes mucus only (10), was unaltered. The latter observers noticed in their dogs that the small intestines were more sensitive to X-rays than the stomach and that degeneration first occurred in the intestinal glands or the crypts of Lieberkuehn and that the mucous cells were the last to degenerate. The cells of the submaxillary gland being chiefly mucous in type, we would expect them to be more insensitive to X-rays than the highly specialized gastic gland which is so sensitive to many factors.

CONCLUSIONS

1. The gastric glands are not stimulated by small doses of X-rays.

2. One hundred and sixty per cent of a "dog erythema dose" when administered to the gastric mucosa with the intervention of the abdominal wall only, will cause a hyposecretion, an achylia, and a marked reduction in pepsin secretion, mucus only being secreted. This is a direct and not an indirect effect.

3. The above dose causes a definite anatomical change in the gastric mucosa which will be described in detail in a later paper.

4. In some animals a peculiar "gastric-juice-like" secretion, free of acid, occurs, which we interpret as being a transudate.

5. The effect of the X-rays manifests itself by a reduction in the acid of the secretion before a change in pepsin content of the secretion.

6. After three or four weeks gastric secretion returns to normal in quality, but is reduced permanently in quantity.

7. The chloride content of gastric secretion is not appreciably altered by X-rays.

8. Our findings do not warrant, but rather contra-indicate, the use of X-rays for treatment of conditions of gastric hypersecretion.

Note: The X-ray equipment used in our work was loaned to us by the Standard X-ray Company of Chicago.

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STUDIES OF THE EFFECTS OF X-RAYS

TABLE I

SHOWING EFFECT OF ONE LARGE DOSE OF X-RAY ON GASTRIC SECRETION DOG WITH PAVLOV POUCH

Procedure	Gastric Secretion				
	Amount in c. c.	Free Acidity per cent	Total Acidity per cent	Peptic Activity mm.	Chlorides per cent
Before X-ray test meal:[1]					
1st hr.	4.5	0.36	0.42	3.0	0.62
2nd hr.	10.0	0.42	0.47	3.5	0.62
3rd hr.	16.0	0.45	0.50	2.5	0.58
4th hr.	13.0	0.45	0.50	2.5	0.68
After X-ray test meal:[1]					
1st hr.	1.0	0.00	0.02	.....	.....
2nd hr.	3.0	0.00	0.02	1.0	.....
3rd hr.	4.5	0.00	0.02	1.2	0.65
4th hr.	8.5	0.03	0.08	2.0	0.65

[1]The test meal consisted of one-half pound of ground round steak.

NOTE: This dog was given the following dose: 110 K.V., 5 ma., 30 cm. focal distance, 1 mm. Al. filter, 6 cm. dia. portal, for one hour. A skin burn was noticed 7 days later. Effect on gastric secretion noted at 10 days.

TABLE II

SHOWING THE EFFFCT OF X-RAYS ON GASTRIC SECRETION IN A DOG WITH A PAVLOV POUCH STOMACH

Procedure	Gastric Secretion				
	Amount in c. c.	Free Acidity per cent	Total Acidity per cent	Peptic Activity mm.	Chlorides per cent
Before X-ray test meal:[1]					
1st hr.	6.0	0.28	0.32	3.5	0.70
2nd hr.	14.0	0.36	0.39	3.2	0.70
3rd hr.	21.0	0.44	0.48	2.0	0.70
4th hr.	10.5	0.43	0.47	2.0	0.65
After X-ray test meal:[1]					
1st hr.	2.5	0.00	0.04	2.0	.....
2nd hr.	4.0	0.09	0.16	1.7	0.65
3rd hr.	7.0	0.09	0.16	2.0	0.62
4th hr.	5.0	0.13	0.22	3.0	.....
					5.20 ma.-min.

[1]The test meal consisted of one-half pound of ground round steak.

NOTE: This dog was given six doses each of Dose I and four doses of Dose II within a period of two months. The dog died of "X-ray toxicosis." A skin burn preceded any effect on gastric secretion by three weeks. One mm. Al. filter was used.

TABLE III

Showing the Effect of X-rays on the Gastric Secretion of a Pavlov Pouch

Procedure	Gastric Secretion				Remarks
	Amount in c. c.	Free Acidity per cent	Total Acidity per cent	Peptic Activity mm.	
Control					
Continuous Meal 1 hr.	1.7	0.16	0.21	....	
1st hr.	9.0	0.20	0.28	3.0	
2nd hr.	8.0	0.31	0.37	2.0	
3rd hr.	7.0	0.30	0.34	1.0	
4th hr.	10.0	0.35	0.39	....	
Two weeks after the last dose *in toto* amounting to 200 per cent "dog's erythema dose" given in a period of eight weeks.					
Continuous Meal 1 hr.	0.7	0	0.03		
1st hr.	0.7	0	0.02		Appetite excellent
2nd hr.	1.0	0	0.03		
3rd hr.	2.5	0	0.07		
Recovery of gastric secretion of pouch four weeks after last dose of X-ray.					
Continuous 1 hr.	0.7	0	0.05	....	Appetite excellent but losing weight gradually
1st hr.	6.3	0.31	0.34	1.5	
2nd hr.	5.0	0.41	0.43	1.0	
3rd hr.	4.6	0.42	0.44	1.0	
4th hr.	5.1	0.41	0.45	0.5	
Gastric secretion five days before death[1]					Appetite good. Dog ate all his meal each day up to the day before death
Continuous Meal 1 hr.	1.7	0.27	0.34		
1st hr.	7.0	0.34	0.42		
2nd hr.	7.2	0.34	0.42		
3rd hr.	9.0	0.36	0.47		

[1]Gross autopsy findings negative. Death due to "chronic roentgen cachexia."

THE DESIGN OF POTTER-BUCKY DIAPHRAGM GRIDS[1]

By R. B. WILSEY

AFTER an experimental study of the various factors governing the performance of the Bucky diaphragm grid, there appeared to be but one feature of design where appreciable improvement could be made on existing models, and that was in regard to the distance between the patient and the film.

It is a well-known principle in radiographic technique that the part radiographed should be as close as possible to the film, in order to obtain the sharpest definition and detail and to minimize distortion. For instance, in the radiography of the frontal sinuses, the forehead rather than the back of the head is placed in contact with the film holder or cassette, and in the radiography of the lumbar spine, the knees are raised in order to lower the arch of the spine and bring it closer to the film. The size of the focal spot and the "undercutting" of scattered radiation both act to diffuse the outlines of portions of the subject which are distant from the film.

Undoubtedly one of the reasons why Dr. Potter succeeded where others had failed in devising a practical form of Bucky diaphragm was that he brought the distance between the patient and the film to the point where it gave improvement in definition as well as in contrast. This factor seems often to be neglected or ignored in the construction of Bucky diaphragms as well as in various types of plate changers. In the models of Bucky diaphragm that the writer has had opportunity to examine, the distance between the cover of the diaphragm and the film ranges from ⅞ inch to 1¼ inches. As a rule, the thickness of the grid does not account for more than half the distance between the patient and the film, so that there is opportunity for reducing this distance by reducing both the thickness of the grid and the free space in which it travels.

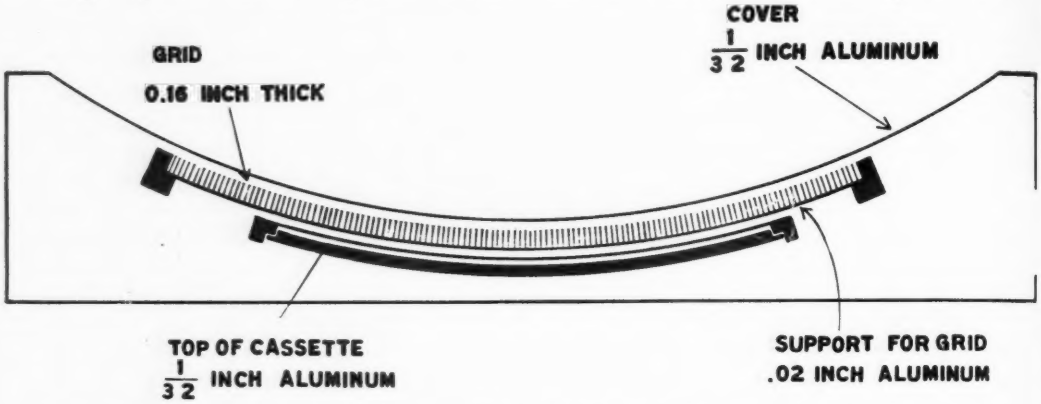
This requirement for the best definition conflicts somewhat with the conditions necessary for high contrast. The highest contrast is secured by making the slits between the lead strips as narrow as possible in proportion to their depth. Since there is a limit as to how close together it is practical to mount the lead strips, the easiest way to secure a small ratio of slit width to slit depth is to increase the depth of the slit; but the experiments showed that to do this, keeping the slit width constant, diminished the definition. The problem in grid design, therefore, is to make the grid as thin and as fine meshed as possible in order to obtain both good definition and high contrast. To secure the same excellence of definition over the whole radiograph, the cassette should be curved to fit the curvature of the grid. The use of the curved cassette with the Potter-Bucky diaphragm has been suggested by Dr. H. W. Van Allen (*Amer. Jour. Roentgenol.*, 1921, viii, 340).

In attempting to put into practice the conclusions of this study, two experimental Bucky grids have been constructed. The first has been described in a recent publication (*Amer. Jour. Roentgenol.*, 1922, ix, 441); the second is an improvement upon the first in that it is a finer meshed grid; placing the lead strips closer together produced a higher efficiency in the removal of scattered radiation, and gave higher radiographic contrast. In the first grid, the lead strips were made ten-thousandths of an inch thick. It was estimated that this thickness should almost completely absorb the scattered

[1]Read before Detroit meeting of Radiological Society of North America, December 5-8, 1922.

rays falling upon them. This grid, with a ratio of slit width to slit depth of 1:3, gave less contrast but better definition than the usual type of grid having thinner lead strips and a smaller slit ratio. It was apparent that the lead strips in this grid were thicker than necessary and that a similar quantity of lead in the form of thinner strips spaced closer together would give a higher efficiency in the removal of scattered radiation. Accordingly, a second experimental grid was built in an attempt to combine a smaller slit ratio with the same short distance between patient and film. Its construction is illustrated in the accompanying diagram. The grid itself is 0.16 (nearly 3/16) inch thick; the lead strips are three-thousandths of an inch thick and are held in place by strips of celluloid twenty-five-thousandths of an inch thick. The ratio of slit width to slit depth is practically 1 to 6. Supporting the grid over its whole area is a sheet of aluminum two-hundredths of an inch thick, fastened at its edges to the aluminum frame. The cover of the diaphragm is of 1/32 inch aluminum, and the top of the curved cassette is also of 1/32 inch aluminum. The clear space to be allowed above and below the grid depends upon how nearly the various surfaces approach true cylindrical surfaces. It was found in this case that when the cover of the diaphragm and the cassette were so adjusted that the grid could travel without touching them, the distance from the upper surface of the cover to the film was ⅜ inch. Probably by increased care in construction this distance could be slightly reduced.

Comparisons of the performance of this grid with that of other models showed clearly the advantage of the thin grid and curved cassette in giving sharp definition and fine detail. Radiographs were made of the same patient with the experimental diaphragm and with one of the usual type, using the same intensifying screens and giving the two films the same development, so that differences in the radiographs were due only to differences in the diaphragms. (Several of these radiographs were shown in the scientific exhibit at the Detroit meeting of the Radiological Society.) The differences in definition obtained in radiographs made with the two types of diaphragms were especially noticeable at the edges of the film, where the curved cassette brings the film much closer to the patient than does the flat cassette. The differences in definition given by the two diaphragms were also shown by radiographing a wire gauze immersed in water; this test avoids any effect of motion upon definition, a possibility which always exists when a live subject is radiographed.



In assembling this experimental grid, considerable difficulty was experienced in getting the lead strips lined up properly, and undoubtedly such a fine meshed grid would be rather expensive to manufacture. The writer would recommend the following dimensions as being the finest and thinnest grid that could be constructed without special difficulty: Thickness of grid ¼ inch; lead strips four or five thousandths of an inch thick separated by strips of wood or celluloid forty or fifty thousandths of an inch thick. With such a grid, the distance between patient and film need not exceed 7/16 inch or ½ inch at the most, which is about half that for the average Bucky diaphragm at the present time. Such a grid would be quite efficient in removing scattered radiation and would give as high contrast as is required for most work; and by reason of the improvement in definition and detail, the usefulness of the Bucky diaphragm would be extended to types of cases where it cannot now be used with advantage.

PAPILLOMATOUS GROWTHS OF THE STOMACH[1]

A Report of Two Cases

By IRVING S. INGBER, M.D., San Francisco, California

PAPILLOMA of the stomach is a comparatively rare lesion, and until recently the scant literature was based almost entirely on necropsy findings. The advent of roentgen ray, with the ability to recognize these growths during the life of the patient, should result in a substantial increase in our knowledge of this most interesting lesion.

Fig. 1, Case 1. Shows a circumscribed defect in pars-media with striations in middle of defect, due to the inter-position of the barium mixture between the villous protrusions.

Pathology. Papillomata are tumors of pavement epithelium with the supporting tissues (connective tissue, and blood vessels) in normal arrangement. The appearance of these tumors may vary. They may be pedunculated with long villous protrusions; they may have a broad flat base with a branching cauliflower formation; they may be single or multiple.

Etiology. The etiology of this lesion is practically unknown.

Course. A benign tumor which may take on malignant characteristics.

Case No. 1. This case was reported to the American Radiological Society about a year ago, but since then I have collected sufficient additional data to warrant reporting it again.

F. W. R., male; occupation, letter carrier.

Previous history. Diphtheria in childhood; normal convalescence; bronchial pneumonia ten years ago.

History of present ailment. Indigestion, and dyspepsia starting about nine years ago. The attacks of dyspepsia were periodical.

The patient stated that with the onset of such an attack, he would regurgitate what he describes as "sweet water." This regurgitation would come on mostly at night between one and two A. M. He would be awakened out of a sound sleep, and regurgitate this so-called white, sweetish watery liquid. During the vomiting attack, according to the patient's description, his stomach would be "tied up into a knot." This feeling would continue for about five minutes after he was through vomiting, and then would be followed by complete relaxation, and general soreness over the entire abdomen.

There was no loss of weight up to the time of his admission to the hospital in November, 1921.

On November 23, 1921, the patient was sent to the X-ray Department for a gastro-intestinal series. The report of this examination was as follows:

The stomach shows the presence of a round, circumscribed defect in the pars-media, situated close to the greater curvature. The defect occupies a space about one and one-half inches in diameter. Both the greater and the lesser curvatures are normal in outline.

[1]Read before the Radiological Society of North America at the Mid-annual Meeting, San Francisco, June, 1923.

The six-hour examination shows no evidence of motility delay, the stomach being empty at this time.

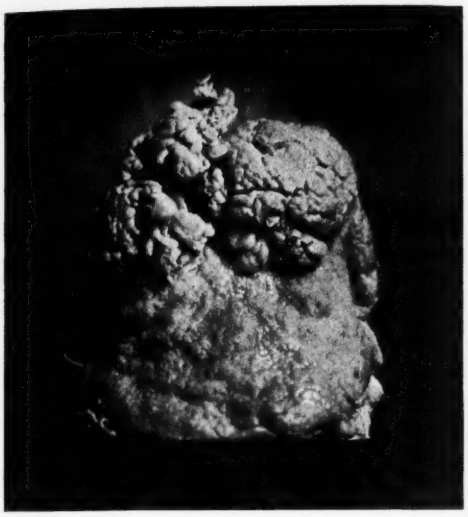


Fig 1-A, Case 1. Shows adeno-papilloma after the removal by gastric resection.

Roentgen conclusions. Polypoid growth of the stomach, situated in the pars-media.

Operation, December 3, 1921. Tumor was found in the anterior wall of the stomach, and was removed by a partial resection of the anterior wall. The patient made a slow, but uneventful recovery.

Pathologist's report. Macroscopically, the growth presents the appearance of a cauliflower the size of a small apple, arising from three slightly separated peduncles. Vertical sections through the peduncle show the gastric wall to be normal from the serosa to the muscularis mucosa. The growth arises as a conglomoration of villous processes from the tunica propria, branching fan-like from the peduncle, the large branches giving off secondary protrusions. The typical glandular structure of the fundus portion of the gastric mucosa is preserved throughout. Vascularization is good. There is no evidence of malignancy.

Diagnosis. Adeno-papilloma of the gastric mucosa; non-malignant.

While the patient has completely recovered from this operation, he has never regained his previous weight; his hæmoglobin is low, never more than 45. There is marked secondary anæmia; appetite is poor. There is more or less of generalized œdema. The loss of weight is not marked, due probably to the fact that the patient has stored up an excessive amount of fluids.

Re-examination, about a year and a half following the operation, shows a recurrence of the growth, a little higher up on the stomach wall than the previous position of the growth, and this time involving the greater curvature.

Fig. 2, Case 1. Shows recurrence one and one-half years after removal of original tumor.

Case No. 2. G. B., male, aged 51; occupation, carpenter.

History of previous complaint. The patient states that first evidence of present condition was about three months previous, characterized by gas eructation, and heartburn, which occurred usually at night after retiring. There was flatulence and bloating, with pain about the umbilicus. Frequent vomiting, thought to be of food taken on day previous; loss of twenty pounds in weight during past three months.

X-ray examination. Large dilatated hypo-tonic stomach with a large fluid level. There is an indefinite filling defect at the pylorus. There is a large gastric residue at seventy-two hours.

Roentgen conclusions. Pyloric obstruction; new-growth.

Operative findings. Pedunculated tumor in pyloric region of the stomach, causing a ball valve obstruction at the pylorus.

Pathologist's report. Pedunculated adeno-papilloma. Non-malignant.

Fig. 3, Case 2. Shows defect in pylorus region of the stomach.

Fig. 4, Case 2. Section through the tumor, and a portion of the pylorus, demonstrating the pedunculated character of the tumor.

Conclusions. The general belief prevalent that all adeno-papillomata of the stomach are of a pre-cancerous nature would seem to be borne out by Case 1. This patient certainly appears to be getting progressively worse, and following a slow malignant course.

Case 2 died several days after operation so that we are unable to comment further as to the malignancy of the growth.

EDITORIAL

M. J. Hubeny, M.D. . . . . *Editor*
Edward W. Rowe, M.D. . } *Associate Editors*
Benjamin H. Orndoff, M.D. }

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RADIOLOGY

Beginning with this issue, RADIOLOGY will be published and controlled solely by the Radiological Society of North America. The decision to publish its own journal was made by the Society in executive session at the San Francisco convention.

The editorial staff and those in charge of the business management of RADIOLOGY will make an earnest endeavor to maintain and improve the already high standards of the past, and ask for the hearty support and co-operation of the subscribers, advertisers, and members of the Society.

CHANGES IN CONSTITUTION AND BY-LAWS

During the Executive Sessions at the San Francisco meeting the following changes in the Constitution and By-Laws were recommended and duly adopted:

Constitution:

Article VI, which reads

"Sec. 1. The Society authorized the formation of a company to be known as The Radiology Publishing Company, Incorporated.

"Sec. 2. The Company and its stock shall be owned and controlled entirely by members of the Society.

"Sec. 3. The Company shall take charge of the proceedings of the Society except as hereinafter provided."

was voted upon section by section and repealed in its entirety, and the following minor changes were made in other places:

Article II, Section 3, to read: "To maintain a journal."

Article V, Section 5, the words "of Radiology" to be deleted so that it now reads: "The President upon assuming the duties of his office, shall appoint his committees and present a record thereof for publication in the next issue of the journal."

Article V, Section 8, the word "journal" to be spelled with a small "j" in two places mentioned, so that it now reads: "The Librarian shall endeavor to provide safe keeping for all records and transactions of the Society, which possess historical value; file and hold subject to reference by the members of the Society, all books and other manuscripts received by the editor and reviewed in the journal; receive and maintain all volumes of the journal; provide proper curation and safe keeping of such museum specimens as he may find it possible to obtain; prepare and exhibit at the annual meeting such articles as he considers advisable; file and list such lantern slides and other articles for reference by the members as in his judgment may be of value. He shall present a yearly report at the annual meeting of the Society."

Article VII to become Article VI.

By-Laws:

Article II, Section 2, delete the words "Journal of Radiology" and substitute "journal" at the end of the clause.

Section 3, the words "Journal of Radiology" to be deleted and the word "journal" substituted.

Article III, Section 1 (a) was changed so that it now reads: "There shall be a publication committee consisting of three members, who shall be appointed by the President of the Radiological Society of North America and who shall serve for a term of three years, one retiring each year. Upon the organization of the Committee the President shall appoint one member to serve for one year, one to serve for two years, and one to serve for three years. The President shall designate who shall be Chairman of the Committee for the first and second years; thereafter the senior member shall be Chairman. In case of vacancy the President shall appoint a member to serve the unexpired term of the member vacating his place on the Committee."

By courtesy of the Santa Fe Railway.

San Francisco Skyline, from the Bay.

THE SAN FRANCISCO MEETING

The Mid-Annual Meeting of the Radiological Society recently held at San Francisco is history. In every way it was a most successful meeting. The business of the Society was transacted with dispatch and harmony. The program was interesting and instructive. The papers were of a high character and the free discussions developed thoughts crowded out of the papers or overlooked by the essayists. For honesty of purpose, sanity of thought, and scientific conservatism, this meeting should go down as a landmark in the story of radiology. A good example is set for other scientific bodies who, after many years of effort, are still distraught by the wrangling of extremists among their members.

In addition to the program, the labors of the committees contributed in a very large measure to the success of the meeting. They brought together the largest and most representative and complete scientific exhibit we have ever had, with plenty of space and good light to display it. The committees, assisted by the profession and citizens of San Francisco, gave unsparingly of their

time, money, and labor to make every member of the Society feel that he was a welcome guest. They left their own work and devoted their entire time to the comfort and entertainment of the members, thus earning for themselves the undying gratitude of the Society and its entire membership.

At the close of the meeting a rising vote of thanks was extended to Doctors Lloyd Bryan, M. P. Burnham, and W. E. Chamberlain, for their faithful performances and untiring efforts, which contributed greatly toward making this meeting a memorable success.

THE ROENTGENOLOGIST AND THE MANUFACTURER

There is, to-day, a growing tendency among the members of the profession to regard the progressive commercial house, not with the attitude of condescension or tolerance so much in vogue between the nouveau riche and "tradespeople," but rather with the spirit of the collaborator or colleague.

Successful men can profit by the work of other successful men in allied branches or industries.

The fact that the manufacturer has something he wants to sell to the doctor does not detract one particle from the fact that the manufacturer has something that will assist the doctor in securing better results.

In the final analysis, it is service that counts. Call it professional or commercial, it is service that counts. And since the manufacturer's service is so closely allied to the physician's rendering the best service to his patients, it naturally follows that whatever the professional man can do to encourage the manufacturer to better and more effective effort, redounds equally and, as must be obvious, the service to the patient must necessarily become more efficient.

The best way in which the roentgenologist can do this is by co-operating with the conscientious manufacturer who for years has put his best effort into everything he makes, by using his goods, by reporting any dissatisfaction to which they may possibly give place, thereby enabling him to take the steps necessary to provide against its recurrence, and, last but not least, by occasionally demonstrating his appreciation in such ways, material or moral, as may occur to him. Mutual respect and consideration should be the bywords.

THE RADIOLOGICAL SPECIAL

Under the direction of William H. Spears, popularly known as "Billy," the special train to the San Francisco meeting, carrying many members of the Society, their wives and mothers, also Messrs. Engeln, Kelley and other illustrious persons, such as Judge O'Hara, was a huge success, worthy of emulation.

Mr. Spears spared no effort for the convenience, pleasure, and entertainment of those fortunate enough to be present. Many pranks were indulged in, good nature prevailing during the entire trip.

AN ENERGETIC MEMBER

Our own Dr. I. S. Trostler is responsible for a good share of the success of the San Francisco meeting. His untiring work in arranging the commercial exhibits and collaborating with Mr. Spears in the conduct of the Radiological Special merits favorable mention. The Society is highly appreciative of all he has done.

COMMERCIAL LABORATORIES

The following report of the Special Committee for the governing of medi-

cal laboratories, so far as it is within the power of the Chicago Medical Society to so govern, has been adopted, as follows:

Report of Committee on Commercial Laboratories

The commercial laboratory has developed as the result of a demand for readily accessible laboratory service at a reasonable price. Their establishment enables the physician to obtain service which otherwise would require the hospitalization of the patient. Laboratories, on account of their close relationship to medicine, should have certain established standards and it is within the power of the Chicago Medical Society to determine what these standards shall be. The present tendency of some laboratories to circularize the lay public with misleading and pernicious literature reflects on the medical profession.

It is perhaps unnecessary to emphasize that laboratory findings cannot replace a careful history and physical examination. Their true function is to furnish diagnostic aid to the attending physician. Rarely do laboratory findings, in and of themselves, constitute a diagnosis, as very few laboratory tests are actually diagnostic. Even tissue examination by itself is often not reliable for tumor diagnosis.

The laboratory report to the physician should be confined to laboratory data. It is not the function of the laboratory to make a clinical examination of the patient.

Laboratories should not advertise tests not yet recognized as of proven value, as results obtained by such tests may mislead the unwary physician.

Direct service of the laboratory to the public is a menace to the proper safeguarding of their health, and should not be permitted.

They should advertise only to the medical profession. Advertising in the lay press or sending literature to the public at large is illogical and misleading and should be prohibited. The literature now circulated by some laboratories gives the layman an exaggerated idea of the value of laboratory findings, and, when negative, an unwarranted assurance of good health.

Extensive ads, including special articles with the so-called purpose of enlightening physicians, should not be tolerated. Special literature distributed to the physician should conform in essentials to the recommendations made by this Committee.

The question has arisen whether laboratories should be permitted to advertise their fees The most important matter is the quality of the service rendered and the physician, we believe, may be trusted to judge whether excessively low fees are consistent with high class service. The profession should be furnished with ade-

By courtesy of the Santa Fe Railway.

San Francisco's New Esplanade at the Ocean Beach, on a November Day.

quate assurance that the reports submitted are based on results obtained by properly trained and experienced workers.

Commercial laboratories, in order to serve the public and profession properly, should have as a director a physician in good standing or a doctor of public health.

Your Committee submits the following specific recommendations:

(1) The director of such laboratories shall be a physician in good standing.

(2) The advertising matter must be moderate in its claim and should avoid advocating medical fads or laying undue stress on the importance of laboratory findings.

(3) Price lists may not be included in the advertisement.

(4) They shall not advertise in the public press, or through circulars, pamphlets, or other agencies to the lay public.

(5) That all those whose names appear in the advertisement, including consultants, are rendering actual service to the laboratory.

(6) That the management, personnel, and equipment be of such a character that honest and accurate work may be expected.

(7) Their activities are to be confined to supplying laboratory data to the profession; treatment to be given only on specific request of the attending physician, and confined to those forms of therapy requiring special equipment or unusual skill, as X-ray therapy and intravenous medication.

(8) Division of fees or rebate between the laboratory and physician is prohibited.

(9) That either a special committee be appointed, or the responsibility be assigned to one of the present standing committees of the Chicago Medical Society to determine which laboratories shall be recognized according to these standards.

R. R. FERGUSON, *Secretary.*

July, 1923.

The above recommendations express the general attitude of the medical profession as regards the commercial perversion of high medical standards. It exemplifies the customary diligence exercised in the execution of the Hippocratic Oath, protecting an unsuspecting public from the avarice of the exploiter.

GENERAL INTEREST

RADIOLOGY is pleased to announce that Dr. Herman Wintz, of Erlangen, Germany, and Dr. Kennon H. Dunham, of Cincinnati, Ohio, Dr. Albert Soiland, of Los Angeles, California, Dr. Henry Schmitz, of Chicago, and Dr. Amedee Granger, of New Orleans, Louisiana, have joined the Editorial Staff as Collaborators.

The Annual Meeting of the American Roentgen Ray Society will be held at Chicago, Illinois, September 18 to 21, inclusive, 1923.

The Rochester Meeting—The annual meeting of the Radiological Society of North America will be held at Rochester, Minnesota, Dec. 4 to 7, 1923. The meeting and exhibits, both commercial and scientific, will be housed in the Methodist Church, which is of ample capacity, and is located only one block from the Mayo Clinic and three blocks from the business section. Rochester is well supplied with first-class hotels, and accommodation will be provided for all members and visitors. In due time every member of the Society will receive a card which he can fill out and return to secure hotel reservations.

Attendance at this meeting promises to be unusually large, and a program of exceptional interest is being arranged. Two full mornings will be devoted to clinics in the amphitheater at St. Mary's Hospital, exemplifying various practical applications of radiology. Among those who will give such clinical demonstrations are Drs. Mayo, Judd, Balfour, Hunt, Hedblom, Adson, Masson, Sistrunk, Pemberton, Henderson, Meyerding, Braasch, Stokes, Gardner, Logan, Moore, Sutherland, Desjardins, and Bowing. An address by Dr. W. J. Mayo will be one feature of the banquet.

The program is filling up rapidly and those who contemplate presenting papers are urged to communicate at once with Dr. L. T. LeWald, St. Luke's Hospital, New York, Chairman of the Program Committee, or the President or Secretary of the Society.

DR. GEORGE M. LUCKEY

It is with a genuine sense of loss to the Radiological Society of North America and to the community which was the scene of his activities, that we chronicle the passing on April 3, 1923, of Dr. George Miller Luckey, of Vinton, Iowa.

Born June 9, 1874, at Hamilton, Illinois, the son of Dr. George J. and Frances Ward Luckey, he followed in the professional path of his father. He was graduated from Knox College, Galesburg, Illinois, in 1897, and from Rush Medical College, Chicago, in 1901. Throughout his college life, he took high rank as a scholar, yet remained a peculiarly unassuming recipient of school honors. For several years he served as President of the Benton County Medical Society.

Dr. Luckey was modest to such a degree that he refused to capitalize on his successes to the extent that his marked abilities entitled him to do. He leaves behind him a record of achievement and respect.

Medical Radiology in Italy—The Fifth Congress of the Italian Society for Medical Radiology will meet at Palermo, Oct. 19, 1923, with Prof. G. Sca-

duto in the chair. The subjects appointed for discussion are "Roentgen-Ray Treatment of Skin Diseases"; "Pneumoradiography," and "Roentgen Rays in Diagnosis of Disease of the Urinary Apparatus." The secretary is Dr. S. Sgroi, Via Alloro 58, Palermo.

Doctor William A. Evans and wife, of Detroit, sailed on the first trip of the *Leviathan* for Europe. They expect to be gone about two months.

Dr. Jno. Anderson, of the London School of Tropical Medicine, was a recent visitor to the roentgen department of the Mayo Clinic. Dr. Anderson will go to Hong Kong to take the chair of Medicine and Radiology in the Hong Kong University.

Army Medical Building Completed—The first building of the Army Medical School, located at the Walter Reed General Hospital, in Washington, is completed and now ready for occupancy. It contains a roentgen-ray unit, laboratories for the various sections and operating rooms.

The first of seven elimination trials to determine Lake Michigan's entry in the Richardson cup race, international Great Lakes yachting event, to be held at Toronto, Sept. 5, 6, and 7, was won by *Yank*, owned by Dr. Hollis E. Potter of the Chicago Yacht club.

Dr. Leo Pariseau, of Montreal, Quebec, paid the department of radiology of the Mayo Clinic. Dr. Anderson will be remembered that Dr. Pariseau was a vice president of the Radiological Society last year.

Dr. Albert Soiland of Los Angeles, Admiral of the Southern California Yacht Club, is aboard his yacht, *Viking IV*, on an ocean voyage of 2300 miles to Honolulu.

Prof. Soret, Paris, aged 69 years, recently had both hands amputated because of malignant disease produced by X-ray burns.

ABSTRACTS OF CURRENT LITERATURE

Hollander, E.: Fallibility of Roentgenologic Evidence of Healed Gastric Ulcer. *Jour. Am. Med. Assn.*, 1923, lxxx, 29.

The changes in the roentgen ray findings of peptic ulcer that take place in the course of medical treatment can be studied best in that type of ulcer showing a penetration on the lesser curvature. When filled by barium, the crater of a penetrating ulcer appears as a bud-like projection from the outline of the stomach, which has been termed a "niche" by Haudek. When situated on the lesser curvature, a niche can be easily visualized, and is unlikely to be simulated by adhesions or cicatrices as are ulcers at the pylorus or duodenum.

Since Hamburger, in 1918, published his roentgenologic studies on the healing of peptic ulcers, several reports have appeared showing the diminution in size or the total disappearance of a niche in response to medical treatment. Most of the reported cases were observed for too short a time to draw definite conclusions regarding their cure, but these changes in the roentgenologic picture were interpreted as strong evidence of healing. The case here reported is instructive in showing the possibility of error in such an interpretation.

It seems reasonable to interpret the diminution in size or the total disappearance of a niche as evidence of healing or cure, especially when these cases are accompanied by clinical evidence of improvement and by other roentgenologic findings such as the disappearance of an incisura and improved motility.

A case reported by the author shows that this interpretation is open to error. From the clinical data in this case a gastric ulcer was diagnosed and roentgen examination disclosed a niche on the lesser curvature. The patient improved under treatment and a later examination showed no evidence of ulcer either on fluoroscopic examination or by means of plates. The case was believed to be one of medically healed ulcer. Symptoms of ulcer again recurred, however, and despite the fact that no roentgenologic evidence of ulcer could be obtained a laparotomy was done. A callous ulcer was found on the lesser curvature as shown in the first roentgenologic examination. This was an indurated ulcer, the crater being filled with a mucoid substance easily removed and without any connection with the ulcer substance. This mucoid material filling the ulcer crater probably accounted for the failure of the barium to enter it in the repeated examinations.

It is difficult to prove the curative effect of medical treatment of chronic gastric ulcer because of the spontaneous remissions in symptoms that so frequently characterize the disease.

Such patients consider themselves cured until a sudden relapse indicates that the disease still exists. However, in such cases, the view is also tenable that the old ulcer had healed, and a new one formed owing to the activity of the original etiologic agent. The study of the changes in gastric secretion or motility that follow medical treatment can give no results that are conclusive of cure, since there are no findings in the secretory or motor functions of the stomach that are pathognomonic for peptic ulcer. Roentgenologic examination (with a small percentage of error in mistaking a projection due to peristalsis or adhesions for a true niche), affords a method of obtaining definite objective record of morphologic changes in the surface of an ulcer.

There are causes for the disappearance of a niche other than the obliteration of an ulcer crater by granulation or cicatricial tissue. As mentioned, food may enter the crater. In the case presented, mucoid material filled the crater. It has been suggested that pressure by œdema or enlargement of an organ, such as the liver or pancreas, adjacent to the ulcer, may obliterate the crater. It must further be borne in mind that, even if an ulcer crater is filled with granulation tissue, the ulcer cannot be considered healed unless its surface is completely covered with epithelial tissue. This condition the roentgen ray cannot demonstrate.

These facts, and also the knowledge that there are frequent remissions in symptoms in this disease, emphasize the need of a long period of observation before drawing any definite conclusions regarding the medical cure of a chronic gastric ulcer.

Bloodgood, J. C.: Tumors of Bone. *Northwest Med.*, 1922, xxi, 308.

Bloodgood says that there are certain differential peculiarities in the X-ray diagnosis of bone tumors. In the case of a patient under fifteen years of age, if the bone lesion is seen to be central, sarcoma may be ruled out and the condition may be considered either as an ordinary bone cyst or a giant-cell tumor, or else perhaps the rare chrondromyxoma. If the radiograph shows the lesion to be periosteal, it is as likely to be a sarcoma as not unless more than one bone is involved, when any malignant lesion may be ruled out. Multiple periosteal lesions are benign, especially in those under fifteen years of age, although later on

these may become malignant. But in a young patient a central lesion may be either benign or malignant.

Syphilis is always suggested by periosteal lesions; in no case of syphilis is there intact bone shell with a central lesion showing as a shadow. Bence-Jones bodies occur in the urine usually only in cases of multiple myxomata and metastasic carcinomata. Myxoma may occur at any age.

Perna, G.: Regarding Ossification of the Acetabulum and the Significance of the Supra-Cotyloidean Tubercle in Man (Sulla ossificazione dell' acetabulum e sul significato del tuberculum supra cotyloideum nell' uomo). *La chir. d. organ. di movimento,* 1922, vi, 485.

There have been many theories in regard to the development of the acetabulum and the author has made a thorough study of the question.

In man three bones are intimately associated in the formation of the walls of the acetabulum. These may be called the anterior, posterior, and superior acetabular bones. The anterior acetabular bone originates from bone nuclei arising at different periods of development, including the lateral and medial iliopubic and pubio-ischiatic nuclei of Staurenghi. The anterior acetabular bone is completely developed about the seventeenth year and invests the lateral extremity of the horizontal branch of the pubis, extending to the ilium; it has a glenoidal and an articular lamina which form a T corresponding to the ilio-pectoral line. After the eighteenth year it fuses with the neighboring bones, the pubis, ilium, and ischium.

The posterior acetabular bone also arises from bone nuclei which appear about the ninth year in the acetabular dorsal cartilage, as well as from other nuclei which appear up to the seventeenth year. When developed it forms a bone wedge between the ilium and the ischium. After the seventeenth year it fuses with the ilium and the ischium.

The superior acetabular bone originates from nuclei in the cephalic segment of the acetabular cartilage where it meets the ilium cartilage. This bone forms the cephalic segment of the acetabular ridge and shows a thick elevation in its anterior surface which constitutes the supra-cotyloidean tubercle. In complete development this bone may be isolated from other articular formations but most frequently is fused with the two bones previously referred to; if such fusion should not occur deep incisuræ occur in the space between the acetabular bones.

The three bones described form the greater part of the facies lunata, the acetabular fundus being developed from the ischium and in part from the ilium.

The superior acetabular bone has a special importance as it is a characteristic of the human species, owing to the important function of the cephalic walls of the acetabulum in the maintenance of the entire trunk in the standing position. The bony ridge in the anterior surface of the superior acetabular bone, *i. e.*, the supra-cotyloidean tubercle above referred to, is also a characteristic of the human species and has functional importance in the erect position. It is evident that the maldevelopment or deficiency of the superior acetabular bone is of particular importance in man and such a defect may reduce the acetabulum to the type found in lower species.

Mayo, C. H.: End-Results in Cancer. *Ann. Surg.,* 1922, lxxvi, 308.

Mayo thinks the action of the roentgen rays and radium rays on the malignant cell is identical, provided that the wave-lengths are equal. In the treatment of malignancy, especially in the cavities of the body, irradiation therapy is most effective when it is applied directly to the tumor, and the roentgen ray when applied to the possible regional and deep metastatic areas. The action of the rays causes a complex physiochemical change in which the cell becomes œdematous, the nuclear substance fragments, and finally all power of cell regeneration is lost. The debris is removed by phagocytosis and replaced by connective tissue. Radium is excellent when vascularity is one of the features of the condition. The end-result of both roentgen-ray and radium treatment is the development of fibrosis and this frequently changes the type of malignancy.

Cohen, J.: Case of Backward Luxation of the Seventh Cervical Vertebra, with Isolated Radicular Compression (Un cas de luxation en arriere de la 7e vertebre cervicale avec compression radiculaire isolee). *Arch. Franco-Belg. de chir.,* 1922, xxv, 945.

In the traumatic case reported the man was not examined until three months after the accident. Radiography then showed a backward luxation of the seventh cervical vertebra with the spinous process approximating the vertebra immediately beneath. Reduction measures failed.

The author remarks that in cervical fractures of this kind, a diagnosis, if made immediately after the traumation, generally assures the success of a manual reduction; but if this should fail the case is at this period more favorable for operation. The earlier the operation the better are the chances for com-

plete restoration. Statistics show that in thirty-one cases of cervical fractures diagnosed radiographically following a traumatism and then treated, there was no death, whereas in thirty-six cases not so diagnosed the mortality was 63 per cent. Radiography, by making an early diagnosis of such fractures possible, permits suitable, effective treatment and prevents later generally irremediable complication.

Alberti, O.: Koehler's Metatarso-Phalangeal Syndrome (La sindrome metatarso-falangea del Koehler). *La chir. d. organ. di movimento,* 1922, vi, 569.

The characteristic X-ray findings in Koehler's metatarso-phalangeal syndrome are, according to Alberti, thickening of the distal part of the second metatarsal, frequently with disappearance of the margin; varying deformity of the metatarsal head suggesting in the early stage desiccating osteochondritis but which later may show widening and flattening of the articular surface; the proximal phalange of the second toe becoming secondarily deformed by widening of its base and of the articular surface; sometimes the periarticular spaces show calcification and osteophytic formations.

Clinically the second toe projects in front of the others.

Pendergrass, E. P., Hayman, J. M., Jr., Houser, K. M., and Rambo, V. C.: The Effect of Radium on the Normal Tissues of the Brain and Spinal Cord of Dogs, and its Therapeutic Application. *Am. J. Roentgenol.,* 1922, ix, 553.

The authors present the results of an experimental study of the effects of radium radiations upon the normal tissues of the brain and spinal cord of dogs both by surface application and implantation. They also give a historical review since Danysz made the first study of the effects of radium upon the tissues of the central nervous system.

The following are the conclusions reached from the experimental work:

1. An exposure of the normal brain tissue up to 1,150 mgm.-hrs. is compatible with life (surface application).

2. The results on the cord, however, would indicate that vital areas of the brain as well as of the cord should never be exposed to surface application or implantation.

3. Microscopic studies indicate that considerable change is to be found with exposures that cause no clinical symptoms.

4. After exposure of 1,000 mgm.-hrs. the brain shows a general swelling throughout the entire radiated hemisphere. This must be ascribed to the production of an œdema which is not limited to the radiated area, but extends throughout the entire hemisphere.

5. Radiation of the brain with radium (surface application and implantation) may cause severe general symptoms which indicate that a powerful toxin has been formed from the radiated tissue.

6. The effect of radium is due to a two-fold action: an effect upon the nucleus and cytoplasm of the cell and the resultant death of the cell under conditions favoring autolysis. The direction of this autolysis is determined by the chief component of the radiated cells. If this is protein, the toxin products of proteolysis may exhibit their general effect. If the chief component is lipoid compounds, the resultant autolysis may free the toxic components of lecithin and produce their characteristic reactions.

7. The use of radium is recommended for the treatment of brain tumors but should be undertaken only by one who is thoroughly familiar with the dangers that may result from its improper use.

8. The findings of the experiments on dogs are applicable to human beings since it is not the destruction of brain tissue that causes death, but some toxæmia. In the application of radium to the treatment of malignant tumors of the brain of man the normal brain tissue should not receive more than 1,150 mgm.-hrs.

As regards radiation in the treatment of brain tumors radium is recommended:

1. As a prophylactic against recurrence after removal of brain tumors.

2. As a prophylactic against recurrence after sella decompression.

3. As an active agent in the treatment of cases of recurrent visual disturbances after sella decompression has been performed.

4. As an active agent by direct implantation into inoperable tumors supplemented by a crossfire radiation through the scalp.

5. As an active agent in cases where brain tumors are only partially removed, by implantation of radium into the center of the cavity and supplemented by crossfire radiation externally.

6. As an active agent by crossfire radiation externally in brain tumors which cannot be localized or discovered by operation.

7. Treatment of spinal cord tumors should be restricted to crossfire radiation by the roentgen ray or radium, as in surface radiation there is great possibility of causing paralysis.

Cheinisse, L.: Radiotherapy as a Means of Treatment of Sterility in Women (La Radiotherapie comme moyen de traitement de la sterilite chez la femme). *Press med.*, 1922, xxx, 977.

It is usually believed that the X-rays have a destructive effect on the ovarian cells, such fact having been fully demonstrated both clinically and by animal experimentation. But the destructive action of the rays is a matter of *dose* and in small dosage the rays have an excitatory effect instead of a destructive action.

At the recent German gynecological congress Thaler and also Flatau reported on irradiation of the ovaries as a treatment of amenorrhœa and other functional disturbances of the ovary. Thaler obtained very satisfactory results in six cases of amenorrhœa and in all these pregnancy ensued within a few months following treatment. However, all these pregnancies ended in abortion.

Flatau employed one-fourth or one-fifth of the erythematous dose as an "exciting" dose. In a series of cases of amenorrhœa or oligomenorrhœa he employed the Coolidge tube, 0.5 mm. copper filter, focal distance 23, intensity 1.8 ma. By means of the Wintz tube the ovarian region was irradiated in front and rear for 5 minutes in each of the two fields. Thirty-eight cases were so treated. In 26 of these Flatau has seen, at the end of from 3 to 6 weeks, menstruation becoming normal, both as regards quantity and duration. In a further series of 12 cases Flatau subjected the whole of the internal genital organs with nerves, vessels, etc., to irradiation with the Dessauer-Warnekros apparatus. Ten of these were cured. In 3 cases pregnancy followed. All were previously sterile.

Linzenmeier of the University Gynecologic Clinic of Kiel has similarly very recently reported the cases of two women who some time after irradiation of the ovaries (in one case for fibroma and in the other for menorrhagia) both became pregnant and were delivered of normal infants at term. In the first case the woman received two irradiations over the right abdomen (10 X over a filter of 4 mm. aluminum). In the second case 20 X filtered through 4 mm. aluminum were applied both abdominally and dorsally. The pregnancy occurred a year later.

In both these cases weak dosage had been used so as not to prevent the possibility of a later conception. Neither of the women previously had had children although married several years. Linzenmeier, in eight cases reported in literature of pregnancy following irradiation, found a malformation of the child in only one case and all developed normally. It was the same in his two personal cases.

Stokes, J. H., and Gardner, B. S.: The Demonstration of Unerupted Hutchinson's Teeth by the Roentgen Ray. *Jour. Amer. Med. Assn.*, 1923, lxxx, 28.

The authors are systematically making roentgenograms of children's teeth in suitable cases in which the delayed appearance of the upper central incisors suggests the possibility of aplasia, such aplasia being considered significant as a clue to the existence of heredosyphilis. They are not yet in a position to make a definite statement with regard to the existence of an actual total aplasia in certain cases of heredosyphilis, but the intra-alveolar demonstration of as yet unerupted Hutchinson teeth, in a case which they report of a baby five months old, seems to be of sufficient diagnostic interest to justify this report. The blood Wassermann reaction of the mother was strongly positive.

In any large syphilologic practice, cases are occasionally encountered in which the fact that the child's teeth are still of the first dentition makes it impossible, in the absence of other conclusive evidence, to clinch the diagnosis of heredosyphilis by the identification of true Hutchinson's teeth. In such cases, it seems possible that intra-alveolar identification of Hutchinson's teeth by the roentgen ray may be of diagnostic service. Moreover, as in the present instance, it may thus be possible to clinch the diagnosis of heredosyphilis in children in whom loss of the first dentition incisors, with delayed eruption of those of the second dentition, makes a direct clinical identification of Hutchinson's teeth impossible for the time being.

It is further of interest to note that, although six arsphenamin injections which this child received at the age of five months caused a prompt recession of the active gummatous manifestations of the syphilis, there was no effect whatever on the germinal anlagen of the Hutchinson teeth. The anlagen of the upper central incisors of the second dentition are recognizable on the average at the twelfth month of life, and presumably have already received the abnormal developmental impulse or trend which leads to the formation of the Hutchinson teeth. It is certainly suggested that treatment for syphilis in infancy cannot affect the appearance of Hutchinson incisors in the second dentition. It must be admitted, however, that the treatment in this case did not reach the intensity demanded by modern standards, so that this conclusion can hardly be accepted as final.

Beclere, M.: Treatment of Uterine Fibromyomata by Means of the Roentgen Rays. *Am. Jour. of Roent.*, 1922, ix, 797.

The statistics of 700 cases of fibromyomata treated by roentgen rays by Beclere show that only 1 per cent of cases was unsuccessfully treated and in only 9 cases was resort to surgery necessary. There are only two questions open to discussion: (1) the contra-indications to the roentgen rays; and (2) the best method for their employment.

In a general way at the present day roentgenotherapy is contra-indicated only in cases in which for some urgent reasons surgical intervention becomes absolutely necessary.

The German theory with regard to the action of the roentgen rays on fibromyomata is best expressed by Seitz and Wintz, who declare that in the treatment of uterine myomata the roentgen rays are efficacious only through their action upon the ovaries. After castration by means of the roentgen rays the retrogression of the myomata takes place in exactly the same manner as after a surgical castration or after the onset of the natural menopause. These authors consider that reduction of the size of the irradiated myomata does not begin until four or five months after the treatment. French radiotherapists hold that the reduction in the size of the myomata after roentgen treatment is quite often more rapid than that which follows the natural menopause and is manifested before the suppression of the menses.

Beclere still holds his opinion, fromerly expressed, that the reduction in the size of palpable uterine tumors begins with the inauguration of the treatment; in most instances it becomes noticeable at the third, sometimes even after the second sitting. From week to week the upper pole of the uterine tumor approaches more or less rapidly the pubic symphysis; in the most favorable cases it may approach at the rate of about 1 cm. per week.

The reduction by irradiation of fibromata which continue to grow after the menopause is a convincing proof of the immediate and direct action of roentgen rays upon fibromyomata of the uterus. Some of the German clinicians of the highest repute now unreservedly acknowledge the direct action of the rays upon myomatous tissues.

The logical result of the French view is the destruction of the myomata without permanent suppression of the menses and the possibility of pregnancy. But practically all these cases result in sterilization because it is impossible to subject the myomatous uterus to the rays without exposing the ovary at the same time. The end-result is, therefore, practically the same by the French or the German method; still the theoretical differences entail differences in technique and treatment.

In the German technique the ovaries are the target toward which all the irradiation must be directed. The French school thinks it necessary to expose to the rays the whole uterine tumor and not to pay any particular attention to the ovaries. But Beclere says that in practice of the German method, as exemplified in Seitz' clinic at Frankfurt, the whole of the uterine tumor is always irradiated.

As regards giving the irradiations in only one or in several sittings—the possibility of destroying at a single sitting and in a few hours the menstrual function and at the same time checking all losses of blood represents from a technical point of view very remarkable progress; but we must take into account the nature of the advantages and the price paid for them and then decide if it is the best method.

Viewed from the standpoint of therapeutic action ovarian sterilization at one sitting does not produce results superior to those obtained with improved modern instruments by the French radiologists with several sittings. The advantages are not of a medical but of an economic nature. Sterilization at one sitting requires that every woman coming under treatment receives uniformly the maximum quantity of the "castration dose" which varies within such wide limits for different individuals that often the minimum would be quite sufficient for bringing about a cure. The majority of patients submitted to this treatment experience a more or less pronounced form of indisposition which the Germans designate as *Roentgenkater* (penetrating irradiation sickness). With smaller doses, given at several sittings, the functional troubles are *nil* or very slight. Besides, repeated sittings offer a better assurance of the progressive destruction of the neoplastic tissues than could be expected from a single sitting. With the newer methods and instrumentation Beclere believes that treatment with small doses given at short intervals, yields the same as, if not superior, results to the one-sitting method of sterilization, taking into account the retrogression of the myomata and the prevention of recurrence; moreover, the patient is not exposed to irradiation malaise or intoxication. The method, however, must often be chosen for reasons other than medical. But for the large majority of cases of uterine fibromyomata, Beclere prefers the treatment with small dose given at short intervals.